

1952 S.A. MEDICAL CONGRESS: JOHANNESBURG, 22-27 SEPTEMBER

South African Medical Journal

Organ of the Medical Association of South Africa



S.-A. Tydskrif vir Geneeskunde

Vakblad van die Mediese Vereniging van Suid-Afrika

Incorporating the *South African Medical Record* and the *Medical Journal of South Africa*

REGISTERED AT THE GENERAL POST OFFICE AS A NEWSPAPER

Vol. 26, No. 34

Cape Town, 23 August 1952

Weekly 2s 6d

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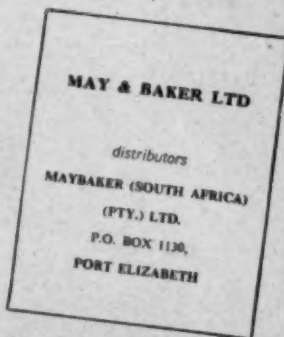
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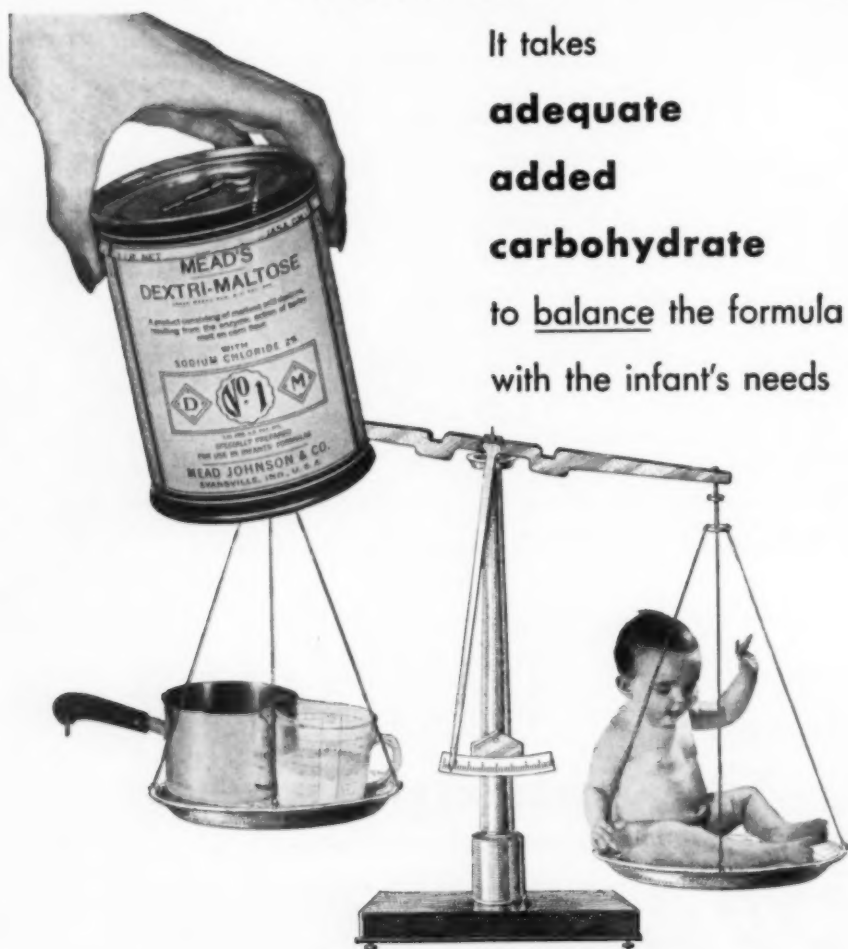
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INSULIN-RESISTANT DIABETES

REPORT OF A CASE WITH AN ASSOCIATED INTERSTITIAL CELL TUMOUR OF THE TESTIS

S. LOPIS, M.D. (RAND), M.R.C.P. (LONDON), M.R.C.P. (EDIN.)

T. H. BOTHWELL, M.B., CH.B. (RAND)

and

J. SWERDLOW, M.B., CH.B. (RAND)

Department of Medicine, University of the Witwatersrand, and the Johannesburg General Hospital, Johannesburg

Since the discovery of insulin by Banting and Best in 1921 it has been noted that certain diabetics require very large doses of insulin for adequate control. Fifty such cases have recently been analysed, but no constant pathological changes have been found at autopsy. Several associated lesions have been described, including fatty infiltration of the liver, haemochromatosis, cirrhosis of the liver, cholecystic disease, pancreatitis, carcinoma of the pancreas, tuberculosis, arteriosclerosis, rheumatoid arthritis and congestive heart failure.¹

In this paper, a case of insulin-resistant diabetes is described, with a previously unpublished associated disease, viz. interstitial cell tumour of the testis. In addition, the subject of insulin resistance is briefly reviewed and a working classification of its causes is presented.

CASE REPORT

A retired army officer aged 69 years was admitted to the Johannesburg General Hospital on 9 June 1948. In 1941 glycosuria had been discovered while he was undergoing a routine medical examination. There were no symptoms of diabetes and the glycosuria was controlled successfully for 7 years with a 1,600 calorie diet. His health remained satisfactory until 3 months before admission, when he developed attacks of nocturnal breathlessness associated with diminished exercise tolerance.

The physical examination was negative except for the finding of a blood pressure of 170/120 mm. Hg, with some cardiac enlargement. The patient's urine was tested 6-hourly for sugar by Benedict's method, but never gave more than a + reaction. The fasting blood sugar was 115 mg. per 100 c.c. X-ray of the chest showed a cardiothoracic ratio of 56%, and on electrocardiography there was a PR interval of 0.26 second with left axis deviation. The patient responded to digitalis, mercurial diuretics and a salt-free diet, and was well enough to be discharged 14 days later. He remained in good health until June 1949, when sugar re-appeared in his urine and his private practitioner instituted insulin therapy with a daily dose of

10 units of Protamine Zinc Insulin. The degree of glycosuria during this period is not known as there was an error in the patient's method of testing urine. However, his general health began to deteriorate, and he was re-admitted to the Johannesburg General Hospital on 31 January 1950 because of increasing breathlessness on exertion and frequent attacks of nocturnal dyspnoea. He had also experienced dryness of the mouth and nausea during the 10 days before admission. During the preceding 18 months he had lost 36 lb. in weight.

He was mentally alert and showed evidence of weight loss. The pupils were normal. The fundi showed 'silver wiring' of vessels but no retinitis. The tongue was dry and furred. The thyroid was not palpable. The respiratory system was normal and there was no evidence of congestive cardiac failure. The pulse was irregular, the rate was 84 per minute and the blood pressure was 180/100 mm. Hg. The maximum cardiac impulse was in the 6th interspace outside the midclavicular line, and the heart was enlarged to percussion. Apart from a generalized Grade III systolic murmur, the heart sounds were normal.

The liver edge was just palpable. The testes were normal in size. There was no clinical evidence of endocrinopathy.

The urine gave a ++++ reaction to Benedict's test and also contained acetone. Thirty units of soluble insulin were given 3-hourly and the urine was constantly free of acetone after 4 days. The symptoms of left ventricular failure were well controlled with mercurial diuretics, digitalis and a salt-free diet. Diabetic maintenance therapy was continued with 150 units insulin daily together with a 1,600 calorie diet containing 160 grams of carbohydrate. On this régime he continued to show ++++ sugar in the urine but remained free of acetone until 10 March 1950. The insulin schedule was again changed, the dose being raised progressively from 40 to 100 units 3-hourly. A fasting blood sugar at this time was 320 mg. per 100 c.c. On an insulin dosage of 800 units daily he continued to have ++++ sugar in the

urine but acetone was absent. Different sites of injection and various brands of insulin were tried, but with the same result.

Many investigations were carried out to ascertain the cause of the patient's resistance to insulin.

LABORATORY DATA

X-ray of the Chest: Unfolding of the aorta with left ventricular enlargement. Lungs normal.

X-ray of the Skull: Osteoporosis. Calcification of the pineal body. No abnormality of the pituitary fossa. Sinuses normal.

X-ray of the Abdomen: Calcification in the region of the left suprarenal gland.

Electrocardiogram: Sino-auricular block. PR interval, 0.22 second. Right bundle branch block.

Full Blood Count: Within normal limits.

Sedimentation Rate: Normal.

Liver Function Tests:

3.9 gm. Albumin per 100 ml.

2.7 gm. Globulin per 100 ml.

Thymol Turbidity Test: 1 Unit.

Thymol Flocculation Test: Negative.

Takata Ara Reaction (Ucko's modification): Negative.

Alkaline Phosphatase: 7.9 Units (King-Armstrong).

Bilirubin: Direct = 0.6 mg. per 100 c.c.

Total = 1.0 mg. per 100 c.c.

Blood Amylase: 124 Units.

Blood Lipase: 423 mg. per 100 c.c.

Stools: Trypsin was present in a 1:5 dilution of the specimen, as indicated by the partial digestion of gelatin. The specimen contained 85% of water; of the total solids 17% was fat; of the total fats 19% was unsat.

Four B.M.R. estimations were within normal limits.

Blood Cholesterol: 130 mg. per 100 c.c.

Plasma Chlorides: 565 mg. per 100 c.c.

Serum Phosphorus: 3.2 mg. per 100 c.c.

17-Ketosteroids in a 24-Hour Specimen of Urine: 6 mg.

Kepler-Robinson-Power Test: Normal.

Various attempts were made to locate some focus of infection in the body. Swabs taken from the tonsils and from prostatic secretions were negative.

On 4 May 1950 an insulin tolerance test was performed after 50 units of soluble insulin had been injected intravenously. No depression of blood sugar from the fasting level of 200 mg. per 100 c.c. was obtained. It was, therefore, decided to investigate whether the patient's serum had any effect on the action of insulin. Two starving rabbits were first tested for sensitivity to 0.2 units of insulin and were later injected with 0.2 units insulin plus 2 ml. of the patient's serum.

RABBIT A

	Blood Sugar Level	
	Insulin (mg. per 100 c.c.)	Insulin and Serum (mg. per 100 cc.)
Before injection	85	100
20 minutes after injection	50	100
40 minutes after injection	55	100
60 minutes after injection	80	105

RABBIT B

	Blood Sugar Level	
	Insulin (mg. per 100 c.c.)	Insulin and Serum (mg. per 100 cc.)
Before injection	85	100
20 minutes after injection	45	100
40 minutes after injection	65	100
60 minutes after injection	80	130

The results of these tests seemed to confirm the suspicion that there was some substance in the patient's serum which was inactivating injected insulin.

In view of this result, and because insulin seemed to be having little if any clinical effect, it was discontinued on 8 May 1950. After 24 hours acetone reappeared in the urine and the patient complained of nausea. Insulin was restarted immediately. An initial dose of 50 units was given, followed by 110 units 5 hours later, and this dose was repeated after a further 8 hours. Although acetone persisted in the urine, there was no serious deterioration in the patient's condition until 9 a.m. on 10 May 1950 when he rapidly became stuporose and markedly ketotic. Vigorous intravenous therapy was immediately instituted, and large doses of insulin were given hourly. The blood sugar level at this time was 1,600 mg. per 100 c.c. and the CO₂-combining power of the blood was 22 vols. %. During the 10 hours that he was in coma he received 1,950 units of insulin, of which half was by the intravenous route. In spite of this his condition continued to deteriorate and he died in deep ketotic coma on the night of 10 May 1950. The blood sugar at death was 1,300 mg. per 100 c.c.

A post-mortem examination was performed about 12 hours after death by Dr. S. Siew of the Pathology Department, University of the Witwatersrand.

SUMMARY OF POST-MORTEM REPORT

The body was that of a thin elderly male subject.

The lungs on section showed congestion, oedema and early patchy bronchopneumonic consolidation. There was a scar present at the right apex.

The heart was enlarged due to hypertrophy and dilatation of both ventricles. The aortic and pulmonary valves were competent but the mitral and tricuspid valves were relatively incompetent. There was some degenerative thickening of the aortic and mitral cusps, but the tricuspid and pulmonary cusps were not thickened. There was severe atheroma of the coronary arteries and of the aorta.

The gums, palate and pharynx were healthy. The stomach showed a hypertrophic chronic gastritis. There was no abnormality of the rest of the alimentary tract and the related lymph glands were not enlarged.

The liver weighed 2,185 gm. The capsule was not thickened and the surface was smooth. On section there was a diffuse fatty change. The gall bladder and bile ducts showed no abnormality.

The vessels around the pancreas were severely sclerosed and atheromatous.

The spleen was enlarged (weight 330 gm.). A chronic perisplenitis was present and, on section, there were multiple small pale foci due to prominence of the lymphoid tissue.

The kidneys were normal in size. The capsules stripped easily leaving finely granular surfaces on which several cysts were present. On section there was slight general cortical atrophy and the vessels were prominent. The renal arteries showed severe atheroma with calcification. Pelvis, ureters and bladder were normal.

The prostate was moderately enlarged due to benign adenomatous hypertrophy. The left testis was slightly enlarged and the normal tissue was completely replaced by a pale soft growth. The right testis was normal.

The brain weighed 1,345 gm. and showed slight senile atrophy.

Microscopic Report. On section of the pancreas there was an increase of fibrous tissue, mostly interlobular in distribution. There was a normal amount of islet tissue and there was no obvious abnormality of the cells.

Section of the left testis showed the presence of an interstitial cell tumour.

Sections of the liver showed the presence of diffuse fatty change.

The adrenal glands were normal.

Kidney sections revealed the presence of benign nephrosclerosis.

The thyroid showed the presence of dilated acini, which

were filled with normal-staining colloid and the epithelial lining was flattened.

On section the lung showed a simple catarrhal bronchopneumonia.

The spleen showed medullary hyperplasia and infiltration with large pale phagocytic cells.

FINAL PATHOLOGICAL DIAGNOSIS

1. An interstitial celled tumour of the left testis.
2. Evidence of hypertension—hypertrophy of the left ventricle, arteriosclerosis and nephrosclerosis.
3. Generalized atheroma.
4. Splenomegaly due to secondary lipoidosis.
5. Terminal bronchopneumonia.

DISCUSSION

In 1929 Root estimated that a depancreatized man weighing 150 lb. would require 200–300 units of insulin daily.² This assumption was based on experimental work in dogs.^{3,4} It is now known that a depancreatized man requires a daily dose of only about 50 units of insulin for adequate control.⁵ In spite of this, Root's figure is still arbitrarily accepted and an insulin-resistant diabetic is defined as 'any non-ketotic diabetic who requires more than 200 units of insulin daily for more than 48 hours to control his diabetic state'.¹ According to this definition, the case described in this paper represents a case of true insulin resistance. Our patient's daily requirements rose to 800 units and even after 14 days on this régime hyperglycaemia and glycosuria persisted.

Despite numerous clinical and laboratory investigations no obvious cause for this resistance could be found during life. Clinically such cases may present difficult diagnostic

(Table 1). This has been divided into short-term and long-term groups. Although the first group does not strictly fulfil the criteria for true insulin resistance, it is of great practical importance, as it includes infection, trauma and poor absorption from the injection site. Ketosis may occur associated with any of these causes or may arise without any obvious precipitating factor. In clinical practice the causes which appear in this group should be excluded before other investigations are undertaken.

Long-term causes of insulin resistance include diseases of the hepato-biliary-pancreatic axis, chief among which are cirrhosis of the liver and pancreatic disease. Over-action of other endocrine glands should be excluded as some hormones antagonize the action of insulin. Thyroid,⁶ pituitary⁷ and adrenal⁸ overaction have all been described in association with insulin resistance.

The major interest of the case described in this paper was the finding of an associated interstitial cell tumour of the testis at autopsy. It is not clear whether this was causally related to the development of insulin resistance in our patient. It produced no obvious signs or symptoms and was not diagnosed during life. Unfortunately only one 17-ketosteroid estimation of the urine was obtained; this was within normal limits. Although experimental results in animals are often not applicable to man, the recent results of Houssay's work⁹ on the action of sex hormones may be of significance in relation to the case reported in this paper. He has shown that diabetes occurs with less frequency in partially depancreatized female rats as compared with male rats. In addition, the incidence of diabetes in both castrated female and male rats is decreased by the administration of oestrone and stilboestrol, while it is markedly increased and the disease made more severe by the giving of the androgens, testosterone and methyl testosterone. From this experimental evidence it would seem that oestrogens may have some protecting action against the development of diabetes whilst androgens may increase its severity. For this reason, interstitial cell tumour of the testis, which may secrete androgens, has been included in our classification.

In a proportion of cases, despite the most searching laboratory tests, no obvious cause for the development of insulin resistance can be found. In such patients it has been suggested that circulating or fixed tissue antibodies to insulin are present.¹⁰ To investigate such a possibility, the hypoglycaemic effects of insulin, on the one hand, and of insulin mixed with the patient's serum on the other, may be compared when injected intravenously into experimental animals. If antibodies are present, then the expected hypoglycaemic response should not be obtained with the insulin-serum mixture. It is of interest that, in the case described in this paper, the expected hypoglycaemic response was not obtained with the insulin-serum mixture. Similar findings have been recorded by other investigators.^{11,12}

It has also been shown that allergy and insulin resistance may co-exist, and that desensitization can lead to the disappearance of both conditions.¹³

The management of cases of insulin-resistant diabetes may prove difficult. Any obvious precipitating or aggravating factor must, of course, be removed. However, in the remaining group where no obvious cause can be found, the treatment is to attempt to control the hyperglycaemic state with very large doses of insulin, as it is probable that

TABLE 1: PRACTICAL CLASSIFICATION OF CAUSES OF INSULIN RESISTANCE IN DIABETES

A. Short Term.

i. Absorption Defects:

- (a) Localized fibrosis or fat atrophy secondary to multiple injections in same site.
- (b) Congestive cardiac failure.
- (c) Shock.

ii. 'Stress' Situations:

- (a) Infection.
- (b) Trauma.
- (c) Surgical Intervention.

iii. Ketosis:

- (a) Arising without obvious cause.
- (b) Secondary to (i) and (ii).

B. Long Term.

i. Disease of the Hepato-biliary-pancreatic Axis:

- (a) Fatty infiltration of the liver.
- (b) Cirrhosis of the liver.
- (c) Haemochromatosis.
- (d) Chronic cholecystitis with or without gall stones.
- (e) Chronic pancreatitis.
- (f) Pancreatic carcinoma.

ii. Over-action of other Endocrine Glands:

- (a) Hyperthyroidism.
- (b) Acromegaly.
- (c) Cushing's syndrome.
- (d) Adrenal cortical tumours.
- (e) Pheochromocytoma.
- (f) Interstitial cell tumour of testis.

iii. Unknown:

- (a) Circulating and fixed tissue antibodies.
- (b) Allergy.

and therapeutic problems. For this reason we have included a classification of the conditions which have been described in association with insulin-resistant diabetes

complete insulin resistance never occurs. For example, one case of diabetic coma was saved with 56,000 units of insulin over a period of 26 hours.¹⁴ For this reason, the insulin dosage to be used in the individual case must be that dose which controls the patient's ketosis and hyperglycaemia. The effective dose may well be an extremely high one and it is possible that our case may have been controlled if heroic doses had been given.

One point of management to be stressed is the danger of the sudden cessation of insulin administration in these cases, even when it seems to be having no hypoglycaemic effect. It has been noted in our case and by others^{12, 13, 16} that the stopping of insulin may be followed rapidly by the onset of an irreversible ketotic coma.

SUMMARY

A case of diabetes in which there was marked resistance to the action of insulin is described. An interstitial cell tumour of the testis was found at autopsy and the possible relationship of this to the development of the insulin resistance is discussed.

A working classification of the causes of resistance to insulin in diabetes is presented and the management of such cases is briefly discussed.

We wish to thank Prof. G. A. Elliott for his advice and encouragement, and Mr. H. D. Barnes of the South African Institute for Medical Research, who performed the biochemical investigations.

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ANNOTATION

TREATMENT OF PARATHION POISONING

Parathion (paranitrophenyl-diethyl-thiophosphate) was first used in South Africa about 4 years ago, for the control of various insect pests. Since then it has been found to be one of the most effective insecticides for the control of certain pests of deciduous fruits and citrus. Parathion is, however, a dangerous poison unless handled with care. Because its popularity is rapidly increasing the chances of Parathion poisoning are also increasing.

It is important to remember that prompt treatment of suspected cases is likely to be successful.

SYMPTOMS

1. *Giddiness, uneasiness, restlessness, anxiety*: These appear as early signs. Severe cases may show ataxia, tremor, drowsiness, mental confusion, slurring speech.

2. *Loss of appetite, nausea*: These are aggravated by smoking and may be followed by muscle twitchings of the eyelids and the tongue.

3. *Vomiting, abdominal cramps, sweating, salivation*: These symptoms come on a little later and will appear if the workman continues working in spite of his having experienced the first group of symptoms.

4. *Diarrhoea, straining and involuntary defaecation, urination, pin-point pupils with blurred vision*: These are very serious signs and indicate a large exposure and absorption.

5. *Bronchial secretion, respiratory distress*: These are likely to occur earlier if material has been inhaled.

6. *Twitchings of face, neck and eye muscles, generalized*

twitchings, muscular weakness: These signs appear in severe cases.

Coma and death occur about 10 hours from the first appearance of symptoms.

In non-fatal cases, symptoms may last for from 12-24 hours. In all cases it is desirable to take the blood pressure which, in the early stages of intoxication, may show a rise but may fall in very severe cases, before death.

The whole symptom complex described above arises from the inactivation of choline esterase with the consequent accumulation and toxic action of acetyl choline.

TREATMENT

1. Most manufacturers of Parathion insecticides label their products as *poisonous*, advising the use of atropine sulphate as an antidote. The usual recommendation is that anyone suffering from Parathion poisoning should take 2 atropine sulphate tablets (grain 1/120 each) if medical aid is not readily available, and that the time should be noted. They are also advised to call immediately for a doctor. Should the doctor not be able to come immediately, this dose of atropine should be repeated at hourly intervals.

2. Subcutaneous atropine injections (grain 1/50 to 1/30) must be given hourly by a medical practitioner until signs of poisoning disappear.

3. Any cases of respiratory distress and later apnoea must be treated with artificial respiration, quickly and persistently.

4. Oxygen has produced temporary benefit but should only be regarded as an adjunct of treatment, and not a main feature.

ABSTRACT

J. A. Rhind: *The Injection Treatment of Hydroceles and Spermatocetes*. (*Brit. Med. Journ.*, 22 September, 1951, pp. 711-713.)

Most of the 145 hydroceles and spermatocetes treated by the injection of quinine-urethane since March 1948 in the General Infirmary at Leeds received only one injection. Pain was reported in less than 10%, and other complications were rare.

Of 128 lesions reviewed, 82 were considered satisfactory in

that they were either free from fluid or contained a small quantity which could be detected only by careful examination. Twenty cases were assessed as failures.

Cases requiring frequent tapping responded better than those whose fluid accumulated only slowly.

Review of the literature suggests that better results may be obtained by the additional injection of lithocaine, but it is doubtful whether the increased disturbance justifies its use in the majority of patients.

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South African Medical Journal

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VAN DIE REDAKSIE

HEMOFILIE: NOUKEURIGHEDE MET DIAGNOSE

Die diagnose van hemofilie kan soms baie maklik wees, maar soms uiters moeilik. Aangesien dit 'n siekte met ernstige genetiese implikasies is, waarby die risiko van chirurgie gedug is, is dit gelukkig dat onlangse verbeterings van hematologiese tegnieke dit moontlik gemaak het om feitlik seker te wees van die diagnose. Twee toetse wat toegepas kan word, is die protrombrien-verbruiktoets en die titrering van beskikbare anti-hemofiliese faktor (anti-hemofiliese globulien) in die plasma.

Die protrombrien-verbruiktoets hang af van die feit dat by die stolling van normale bloed in glasbuis meeste van die protrombrien-aktiwiteit van die plasma verdwyn en baie min bly oor in die resultante-serum. As die klontvorming van die bloed vir een of ander rede onvolkome is, mag daar 'n sekere mate van protrombrien aktiwiteit in die serum gevind word. Die twee algemene hemorragiese toestande waarin dit voorkom is hemofilie en trombosietopeniese huidbloeding. Die protrombrien-verbruiktoets bewys selfs in die aanwesigheid van 'n normale stollingstyd 'n stollingsgebrek en is 'n meer sensitiewe toets van die funksie van klontvorming. In feitlik alle gevalle van hemofilie word abnormale resultate met hierdie toets verkry.

In gevalle van hemofilie met 'n verlengde stollingstyd is die toets op beide aar- en haarvatbloed positief. In die buitengewone gevalle van hemofilie met 'n normale stollingstyd, is die toets slegs positief op serum wat van aarbloed verkry is. Aangesien die stollingstyd in die meeste gevalle van hemofilie verleng is, kan 'n redelike seker diagnose verkry word met 'n kombinasie van 'n verlengde stollingstyd van haarvatbloed en abnormale protrombrien-verbruik op haarvatbloed getoets. Dit is van groot waarde as daar vir enige rede nie aarbloed verkry kan word nie, bv. by suigeling. Daarenteen, as 'n voldoende aarprik uitgevoer kan word, is 'n verlengde stollingstyd, op sigself, 'n goeie leidraad tot die diagnose van hemofilie.

Die tweede toets wat toegepas kan word, is die titrering van die hoeveelheid beskikbare anti-hemofiliese faktor in die bloed. As 'n klein hoeveelheid normale bloed by bevestigde hemofiliese bloed gevoeg word, word die stollingstyd van laasgenoemde aansienlik verkort. Die bloed van die pasiënt wat getoets moet word, sal slegs die stollingstyd van bekende hemofiliese bloed kan beïnvloed tot die mate waarin dit beskikbare anti-hemofiliese globulien bevat. As die pasiënt aan hemofilie ly, sal sy bloed of

EDITORIAL

HAEMOPHILIA: REFINEMENTS IN DIAGNOSIS

The diagnosis of haemophilia can at times be very easy, but at other times nothing may be more difficult. Since it is a disease with serious genetic implications, in which the risk of surgery is formidable, it is fortunate that recent refinements of haematological technique have made it possible to be practically certain of the diagnosis. Two tests which can be applied are the prothrombin consumption test and the titration of available antihemophilic factor (antihemophilic globulin) in the plasma.

The prothrombin consumption test depends on the fact that in the coagulation of normal blood in glass tubes most of the prothrombin activity of the plasma disappears and very little remains in the resultant serum. If for any reason the clotting of the blood is defective, a certain amount of prothrombin activity may be found in the serum. The two common haemorrhagic states in which this occurs are haemophilia and thrombocytopenic purpura. The prothrombin consumption test demonstrates a coagulation defect even in the presence of a normal coagulation time and is a more sensitive test of clotting function. Abnormal results are obtained with this test in practically all cases of haemophilia.

In cases of haemophilia with a prolonged coagulation time, the test is positive on both venous and capillary blood. In the rare cases of haemophilia with a normal coagulation time, the test is positive only on serum obtained from venous blood. Since in most cases of haemophilia the coagulation time is prolonged, a reasonably certain diagnosis can be reached by a combination of a prolonged capillary blood coagulation time and abnormal prothrombin consumption tested on capillary blood. This is of great value when for any reason venous blood cannot be obtained, e.g. in infancy. On the other hand, if an adequate venipuncture can be performed, a prolonged coagulation time is, by itself, a good guide to the diagnosis of haemophilia.

The second test which can be applied is the titration of the amount of available antihemophilic factor in the blood. If a small proportion of normal blood is added to known haemophilic blood, the coagulation time of the latter is shortened considerably. The blood of the patient to be tested will be able to affect the coagulation time of

geensins die stollingstyd van bekende hemofiliese bloed verkort nie of as dit enige uitwerking het, sal dit baie minder wees as dié van 'n gelyke hoeveelheid normale bloed.

Die moeilikheid met die uitvoering van hierdie toets is dat dit bekende hemofiliese bloed vereis. Die toets kan omgekeerd uitgevoer word deur 'n klein hoeveelheid normale bloed by die pasiënt se bloed te voeg. As dit die stollingstyd van laasgenoemde verkort, bewys dit dat die pasiënt gebrek het aan 'n faktor wat normale bloed bevat. Gewoonlik beteken dit 'n tekort aan anti-hemofiliese globulien.

Die toevoeging van normale bloed tot hemofiliese bloed verbeter ook die protrombien-verbruikgebrek daarvan en kan gebruik word met die toetsing van beskikbare anti-hemofiliese globulien; maar die verkorting van die stollingstyd is gewoonlik 'n eenvoudiger aanduiding en in meeste gevalle heeltemal voldoende.

As die pasiënt se bloed op die omskrewe wyse reageer, word dit vermoed dat beskikbare antihemofiliese globulien ontbreek en dat die pasiënt aan hemofilie ly.

known haemophilic blood only to the extent to which it contains available antihemophilic globulin. If the patient has haemophilia, his blood will either not shorten the coagulation time of known haemophilic blood at all, or, if it does have some effect, this will be far less than that of an equivalent proportion of normal blood.

The difficulty in doing this test is that it requires known haemophilic blood. The test can be done in the reverse manner by adding a small proportion of normal blood to the patient's blood. If this shortens the coagulation time of the latter, it demonstrates that the patient lacks a factor which normal blood contains. This usually means a shortage of antihemophilic globulin.

The addition of normal blood to haemophilic blood also improves its prothrombin consumption defect and this can be used in assaying available antihemophilic globulin; but the shortening of the coagulation time is usually a simpler indication and in most cases perfectly adequate.

If the patient's blood behaves in the manner outlined, it is presumed to lack available antihemophilic globulin and the patient to have haemophilia.

DIE GEBRUIK VAN UREA-MENGSEL AS SPOELMIDDEL

IN TRANSURETHRALE RESEKSIE VAN DIE PROSTAAT

L. P. MAAS, M.B., Ch.B.

Pretoria

Die sogenoemde transurethrale reseksie oligurie-sindroom was een van die mees bespreekte onderwerpe gedurende die laaste 3 jaar.

Oligurie-sindroom. Hierdie entiteit vergelyk geensins met die gewone post-operatiewe oligurie wat aangetref word na onveranderbare skoktoestande nie.

Dit is 'n alombekende feit dat sommige gevalle waar 'n pasiënt wat in 'n goeie pre-operatiewe toestand verkeer het, kort na reseksie die volgende simptomebeeld toon. Die simptomebeeld word gekenmerk deur nausea, anorexia, rigors, ruggyn, anemie—wat nie verklaarbaar is deur die bloedverlies gedurende die reseksie nie—oligurie en 'n progressiewe azotemie en 'n mate van non-obstruktiwe geelsug.

Skygbaar kom hierdie toestand veral voor in die gevalle waar die reseksie betreklik lank geneem het en veral waar die periprostatische veneuse pleksusse oorgesny is met taamlike erge bloeding vanuit hierdie sinusse. Die bloeding van hierdie veneuse pleksusse is ook uiters moeilik om te beheer met die gevolg dat etlike minute van aanhoudende fulguratie van die bloeipunt en 'n verhoging van intra-urethrale druk soms nodig is om die bloeding tot stilstand te bring. Dit beteken tegelyk 'n oorvulling van die blaas met die spoelmengsel vir daardie selfde periode. Wat skygbaar tydens hierdie tydperk gebeur is dat daar van die spoelmengsel in die veneuse sinusse geforseer word deur die verhoogde intra-urethrale druk.

Patogenese. Die patogenese van hierdie sindroom is tans nog nie baie duidelik nie. Dit is moontlik dat intravaskulêre hemolise van die rooieselle, of die infiltrasie

van die peri-prostatische weefsel deur die nie-isotoniese spoelmengsel 'n spesifieke renale reaksie teweegbring.

McLaughlin postuleer die moontlikheid dat daar 'n spesifieke nefrotoksiese stof vrygelaat word wanneer die prostaatweefsel vir 'n lang tydperk blootgestel word aan 'n intensiewe fulguratie met 'n hoë frekwensiestroom. Hierdie stof kom ooreen met histamine in sy spastiese effek op spierweefsel en mag dus vasospasme van die renale vate veroorsaak en sodoende renale isemie. Die renale stoornis kan moontlik ook teweeggebring word deur die sirkulasie kortsluiting wat beskryf is deur Trueta.

Emmett en Foley het afsonderlik kortgelede bewys dat daar wel intravaskulêre hemolise voorkom wanneer steriele water gebruik word as spoelmengsel, gedurende 'n reseksie.

Foley het selfs rooigekleurde urine gesien uitspuit deur die ureteropeninge gedurende 'n reseksie, en het 'n groot hoeveelheid vry hemoglobine in die bloedplasma van die pasiënt gevind net na die reseksie. Sodoende het hy sy hipotese bewys dat die urine nie alleen deur bloed van die prostaatbed gekleur is nie; maar ook deur vry hemoglobine.

Alhoewel hemolise plaasvind is dit aan die anderkant weer bewys dat daar geen, of min, slegte gevolge in pasiënte voorgekom het na binne-aarse inspuiting van groot hoeveelhede hemoglobine-mengsels.

Nieteenstaande die feit dat die meganisme van die toestand nie juis duidelik is nie, weet ons egter dat in die sindroom daar 'n erge mate van anemie met hemoglobinemie en hemoglobininurie voorkom, wat later oorgaan

in 'n laer nefron nefrose soos gesien word in gevalle van swartwaterkoors, onverenigbare bloedoorgietings, en in gevalle van swaar brandwonde.

Volgens Flink kom vry hemoglobine in die urine voor wanneer die konsentrasie van vry hemoglobine in die plasma die 135 tot 290 mg. per 100 c.c. merk oorskry. Dit verdwyn uit die sirkulerende plasma in 36 uur. Ongeveer een-derde word deur die niere uitgeskei terwyl die res deur die retikulo-endotheelsisteme verwyder word. Laasgenoemde verander dit waarskynlik in pigment wat die oorsaak van die geelsug is.

Wanneer die vry hemoglobine in aanraking met die niere kom veroorsaak dit vasokonstriksie. Die vasokonstriksie veroorsaak weer 'n verlengde kontak tussen die hemoglobine en die tubuli, wat verder as gevolg het 'n verlengde uitskeiding van die hemoglobine en 'n vermeerdering van die toksiese effekte van die vry hemoglobine.

Indien die niere alreeds bekadig is deur arteriosklerose, hidronefrose, of pyelonefritis, en as renale vasokonstriksie alreeds teenwoordig is as gevolg van bloedverlies, of 'n val in bloeddruk, kan 'n mens maklik die verergerde effek van vry hemoglobine op die niere gedurende transurethrale reseksie verstaan.

Die veranderinge wat teweeggebring word in die nier sluit in nekrose-deskwamiasie van die epitheel van die distale deel van die buise, voorkoms van gepigmenteerde silinders in hierdie en in die opvangbuis, en neerslag van hemosiderin in die kronkelbuis.

Dit is egter nog nie heeltemal duidelik of die verslegte nierfunksie te wyte is aan die verstopping van die buise deur hierdie silinders, en of dit as gevolg is van die direkte toksiese effek van die vry hemoglobine of sy afvalprodukte op die buise, of as gevolg van sirkulasiestoornis nie.

Al hierdie faktore speel skynbaar 'n belangrike rol. Die veranderinge is herstelbaar tensy dit baie ekstensief is.

Profilakse. Hierdie siektetoestand is egter voorkombaar deur te verhoed dat die volgende faktore teenwoordig is gedurende die reseksie:

(a) Oorvulling van die blaas.

(b) Langdurige fulguratie van die bloeipunte.

(c) Diep disseksie in of deur die prostaatkapsel.

(d) Die gebruik van hemoliserende spoelmiddels.

Nesbit en Gluckman het alreeds vroeg hierdie oligurie-sindroom herken en om dit te verhoed het hulle in plaas van steriele water 'n 1.1% oplossing van die aminosuurglisien wat in oplossing is, as spoelmengsel gebruik. Hulle het geen hemolitiese reaksie in 'n 1,000 gevalle van transurethrale reseksie gehad nie.

Hierdie skrywers het dan ook die volgende punte neergelê waaraan die ideale spoelmengsel moet voldoen:

(a) Die spoelmengsel moet isotonies, of non-hemoliserend wees in hipotoniese konsentrasies. Steriele water voldoen nie aan hierdie vereistes nie. Glukose is non-hemoliserend in oplossing sterker as 2%. Glisien is isotonies in 2.1% oplossing en non-hemoliserend in konsentrasie hoër dan 1%. Urea is isotonies in 'n oplossing van 1.8%.

(b) Die mengsel moet non-elektrolities en net baie ligtelik ioniseerbaar wees. Al die mengsels voldoen aan hierdie vereistes.

(c) Die mengsel moet geen toksiese effek op lokale weefsel hê wanneer dit intraveneus toegedien word nie. Steriele water het 'n toksiese effek en kan hemolise ver-

oorzaak, terwyl glukose, glisien en urea aan genoemde vereiste voldoen.

(d) Die mengsel moet helder wees sodat die deurskynendheid maksimaal kan wees. Water is helder. Glukose, glisien en urea word relatief minder helder daar dit die bloedselle in 'n suspensie hou. Hierdie karaktertrek is relatief gesproke 'n voordeel, daar dit bloedbeheer vergemaklik.

(e) Die stof wat gebruik word ter vervaardiging van die spoelmengsel moet goedkoop en maklik verkrygbaar wees in groot hoeveelhede. Alvier die genoemde bestanddele voldoen aan hierdie vereiste.

Glukose in isotoniese oplossing het veral een nadeel, nl. dat dit die instrument en alles waarmee dit in aanraking kom taai en klewerig maak. Hierdie ongewenste faktor is nie teenwoordig wanneer daar gebruik gemaak word van urea as spoelmengsel nie. Urea in poeivorm is betreklik goedkoop en groot hoeveelhede kan verkry word teen 2s. 6d. per pond.

Die spoelmengsel word maklik vervaardig deur een pond urea met water te meng en te kook totdat 1 pint van die gekonsentreerde oplossing verkry is.

Van hierdie gekonsentreerde oplossing word 1 ons by 1 pint steriele water gebruik om die gewenste 1.8% oplossing te kry.

Die hoeveelheid spoelstof per reseksie varieer en hang af van die grootte van die klier en die tyd wat die reseksie duur.

Gemiddeld word ± 4 gallon water gebruik met elke transurethrale reseksie. Die hoeveelheid urea dus benodig per reseksie varieer van 1 tot 1½ pond.

Ons kan dus sien dat die onkoste verbonde aan die gebruik van hierdie spesifieke spoelmengsel uiters gering is en 'n goeie rede mag wees waarom urea gebruik word in plaas van die ander duurdere stowwe.

Ervaring. Sedert die begin van 1949 tot April 1950 is 200 gevalle met vergroting van die prostaat transurethraal gedoen in die Pretoria Algemene Hospitaal. In hierdie 200 gevalle was die spoelmengsel in elke geval steriele water. Ses van hierdie 200 gevalle het na die reseksie die oligurie-sindroom getoon. Twee gevalle het volkome herstel met roetiene-behandeling terwyl 4 beswyk het.

Sedert April 1950 tot tans is 127 gevalle gedoen met 'n 1.8% urea-mengsel. In geen van hierdie gevalle het die oligurie-sindroom ontwikkel nie.

Ongeukkig is die serum hemoglobine nie gedoen tydens die gebruik van steriele water as spoelmengsel nie.

In 7 gevalle is die serum hemoglobine gedoen na die reseksie tydens die gebruik van urea-mengsel en in nie een van die gevalle was die serum hemoglobine meer as 20 mg. per 100 c.c. nie, terwyl Creevy en Lander rapporteer het dat die serum hemoglobine in gevalle waar die spoelmengsel steriele water was tot so hoog as 490 mg. per 100 c.c. onmiddellik na die reseksie was.

Onder al die verskillende non-hemoliserende spoelmengsels in gebruik vind ons urea-mengsel die beste.

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THE TERRAMYCIN TREATMENT OF GONORRHOEA WITH TWO GRAMMES OVER FORTY-EIGHT HOURS

R. R. WILLCOX, M.D.

St. Mary's Hospital, London, W.2

A number of workers have now undertaken pilot studies of the effects of Terramycin in the treatment of acute gonorrhoea. *In vitro* experiments by Gocke *et al.*^{1,2} who tested numerous strains of gonococci against a number of antibiotics, indicated that Terramycin ranks with Aureomycin next to Penicillin in effectiveness. Caldwell *et al.*³ had no failures in 7 patients treated with Terramycin over 4-5 days, and Perdrup⁴ treated 5 cases successfully with the relatively high dose of 4 gm. given over 24 hours.

The fact that the drug is also potent against syphilis, however, has prompted most workers to try to determine the minimal effective dose. Single doses of up to 2 gm. would appear to be insufficient. Hendricks *et al.*⁵ had only 15.55% success with single doses of 250-1,500 mg. Schoch and Alexander¹¹ treated 26 cases with single doses of 1 gm. but 3 patients still showed gonococci at 24 hours. Putkonen⁶ treated 12 women with single doses of 0.5 gm. with 6 failures, although 45 (62%) were considered cured with single doses of 1 gm. Robinson,¹⁰ using single doses of 1 gm., had 3 failures in 6 patients although 14 of 18 treated with single doses of 2 gm. were apparently cured. Willcox¹³ likewise had 3 failures in 6 patients given single doses of 1-2 gm.

Greater success has attended treatment with divided doses. Hendricks *et al.*⁵ treated 15 patients with 2 doses each of 500 mg. given 6 hours apart, with 8 successes. All of 15, however, were claimed as cured when 2 doses of 1 gm. were given at the same interval. In Britain, Willcox¹⁴ treated 23 patients with this régime. Of 19 followed there were 2 relapses, one re-infection and 2 with non-specific infections. Likewise Beinfeld *et al.*¹ treated 54 cases with 0.5 gm. given every 4 hours for 4 doses (2 gm. in all). There were only 3 failures, and only one failure in 16 others given a total of 750 mg. in 2 doses 4 hours apart.

The present paper describes the results of treatment of 44 patients with acute gonorrhoea with an economical dose of 2 gm. spread over 48 hours, a régime which has not so far been described.

THE CASES

Forty-two of the patients were male and 2 were female, 9 were married and 35 were single. The average age was 29.9 years (extremes 20-51). Five of the males were Jamaican or West African Negroes and the remainder were white Europeans.

Twenty-two (50%) of the patients had suffered from venereal disease before the present attack. Histories were obtained of 22 attacks of gonorrhoea, 5 of non-specific urethritis and 2 of syphilis. As has previously been pointed out¹² the Negro in London is particularly prone to infection. The 5 male Negroes owned to 8 previous episodes (1.6 each), whereas the 37 white males shared the remaining 21 (average 0.57 incidents each).

Although 28 of the patients attended on the first or

second day of the disease, the over-all average duration of the discharge before treatment was 3 days (extremes 1-14). Dysuria was noted in 21 cases. Gonococci were readily isolated in smears from all.

The Wassermann and Kahn serum tests were negative in all. The gonococcal complement fixation test was performed on 36 patients, the results being positive in one, doubtful in one and negative in 34. This bears out the contention of Cooper *et al.*³ that this test has lost its value as a routine measure in the management of acute gonorrhoea, as the disease is usually diagnosed, treated and cured long before it has a chance to become positive.

The Treatment. Treatment consisted of one 250 mg. capsule of Terramycin given orally after meals 4 times a day for 2 days. No significant toxic effects were noted. One patient had some diarrhoea, one became languid and suffered from temporary anorexia, and another had a mild attack of the ano-rectal syndrome which has been described.¹⁵ In none was any interference with the treatment found to be necessary.

Results. Of the 44 treated 6 defaulted at once and were not seen again. The remaining 38 attended for an average of 3 post-treatment visits over an average of 30.4 days each (extremes 4-86).

Successes. Twenty-seven patients (71%), who were watched over 1-7 (average 2.8) post-treatment checks over 4-66 (average 26.3) days, remained clinically and pathologically well with clear urines and urethral and/or prostatic smears free from pus. Only 7 of these patients were observed for periods of 2 weeks or less.

Re-infections. There were 4 re-infections (10.5%).

One patient whose clinical status was entirely satisfactory at 7, 23, 29 and 63 days reported with a new discharge containing gonococci at 86 days. The consort was examined and was found also to be suffering from gonorrhoea.

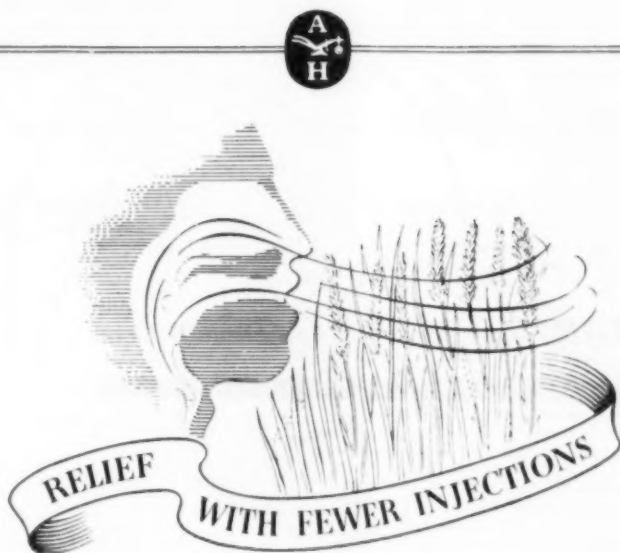
Another patient, satisfactory at 4 days, reported with a re-infection at 14 days apparently obtained from the original consort. He was re-treated with the same schedule, the consort was attended to, and he was quite well 39 days after the second treatment.

Another, satisfactory at 2 days, defaulted until the 49th day when he reported with a fresh discharge also apparently acquired from the original consort. He was re-treated as before but did not subsequently attend again.

The fourth patient, reporting with a fresh discharge on the 25th day, was re-infected from his wife who was also shown to be carrying gonococci.

Non-Specific Infections. Four patients had non-specific infections (10.5%).

In the past there has been a tendency to classify these cases as 'failures'.⁸ The only true criterion of failure is the rediscovery of the gonococcus by smear or culture in cases in which re-infection cannot reasonably be inferred. In the opinion of the writer the majority of these non-



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RATIONALE :

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To eliminate pain and infection.

RESPONSE :

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REFERENCE :

*Reid, W. Ogilvy, Brit. Med. J. I. (1946) 648.

CHRONALGICIN in chronic Otitis Media

RATIONALE :

To dissolve debris, deodorise, improve drainage and eliminate infection, at the same time to dry and harden the meatal skin.*

RESPONSE :

Improvement is noted early, but treatment may be necessary for some weeks before activity ceases or dry ear results.

REFERENCE :

*Reid, W. Ogilvy, Brit. Med. J. I. (1946) 648.



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specific conditions which follow the treatment of gonorrhoea with antibiotics are in reality concomitant infections with non-specific urethritis which frequently has a more variable and longer incubation period than gonorrhoea. The response to treatment of these 4 cases only substantiates this view.

One patient was clinically satisfactory at 5, 12, 32 and 39 days, but at 54 days presented a muco-purulent discharge in which gonococci were not found. There was no history of re-exposure. The discharge failed to clear after 4 daily injections of 1 gm. of Streptomycin and 3 daily injections of 600,000 units of Penicillin. It subsequently responded to Chloramphenicol.

Another, satisfactory at 2, 7 and 14 days, showed a non-specific urethritis at 21 days but without a history of re-exposure. This was successfully treated with Aureomycin.

Another, clinically satisfactory at 2, 7, 23 and 35 days, suddenly showed pus cells in the prostatic bead at 49 days and at 63 days. No gonococci were isolated.

The fourth, satisfactory at 5, 12, 19 and 26 days after treatment, had a non-specific discharge at 35 days which responded satisfactorily to Terramycin given for one week.

Failures. There were only 3 definite failures (8%).

One patient had relapsed by the fourth day when gonococci were found in the smear. He was re-treated with the same dosage and was satisfactory at 2, 29, 36 and 47 days. He attended with a further re-infection on the 69th day from re-treatment and his consort was shown to have gonorrhoea.

Another again showed gonococci on the eighth day, was re-treated with the same dosage but did not attend again.

The third patient showed gonococci at 7 days and was then given 300,000 units of Procaine Penicillin. He responded to this but subsequently developed a muco-purulent discharge not containing gonococci and was treated with Streptomycin. This is an example of a non-specific infection developing after Penicillin.

The results are summarized in Table I.

TABLE I: TREATMENT OF GONORRHOEA WITH 2 GM. OF TERRAMYCIN GIVEN OVER 48 HOURS

Treated	Followed	Cured	Reinfections	Non-specific Infections	Definite Failures
44	38	27 (71.0%)	4 (10.5%)	4 (10.5%)	3 (8.0%)

SUMMARY AND CONCLUSIONS

1. Forty-four patients, all but 2 male, were treated with 2 gm. of Terramycin given in 8 divided doses over 48 hours.

2. Of 38 followed, the clinical progress of 27 (71%) was without incident. In addition there were 4 re-infections and 4 patients with non-specific infections.

3. It is considered that the latter should not be regarded as treatment failures but rather as concomitant infections with non-specific urethritis.

4. There were only 3 definite failures (8%).

5. It is considered that the results of treatment with Terramycin in the dosage given are comparable with those obtained with Penicillin, and when given in this manner the antibiotic is also as free of adverse side-effects.

6. No less than Penicillin, however, Terramycin may mask syphilis although with the accumulation of experience this risk may be considered to have been exaggerated. The dose of Terramycin given in this series is, as regards the serum levels obtained, probably comparable with a dose of 600,000 units of Procaine Penicillin and this aspect should therefore be borne in mind in later studies.

7. When Terramycin is in more plentiful supply and its price compares more favourably with that of Penicillin its simple mode of administration may in the end result in it replacing Penicillin in the routine treatment of gonorrhoea.

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SPERMATOGENIC REBOUND PHENOMENON

AFTER TESTOSTERONE ADMINISTRATION

P. J. M. RETIEF, M.B., Ch.M.

Cape Town

To those interested in the treatment of male infertility, this new concept holds great promise. Heller *et al.*¹ Heckel^{2, 4} and Heckel *et al.*³ have shown that whereas male hormone administered to males promptly results in marked depression of spermatogenesis, this is followed

some months later by a reactive phase characterized by remarkable stimulation of spermatogenesis. This reactive phase is known as the 'spermatogenic rebound phenomenon'.

Recently^{5, 6} I outlined the principles of therapy for

cases of male infertility and pointed out that for the condition of oligozoospermia* (the group in which the great majority of infertile males fall), the treatment was in the main most unsatisfactory, if not useless. This statement now needs to be qualified, and we await with great interest the outcome of this new line of therapy.

The remarkable regenerative changes in the testes which eventually follow testosterone administration are incontrovertible. Whether the hazards of the therapy outweigh the benefits derived and whether the fertility index is sufficiently raised to produce the ultimate aim of pregnancy, remain to be seen. Because this therapy has certain limitations, and indeed hazards, a timely evaluation is called for. It would be a pity if a valuable therapeutic aid in a heretofore almost hopeless condition should fall into disrepute because of faulty application.

Heckel² showed that testosterone affected spermatogenesis adversely, as judged by semen analysis. This was confirmed in varying degrees by many other observers, so that the use of testosterone for male infertility was with justification frowned upon. It was a chance observation which led to the recognition of its potential value. Heller³ and his co-workers conducted a critical examination into the short- and long-term effects of testosterone on the histology of the testis. They were aware of its depressing action and were interested whether the effects would be permanent. They unexpectedly discovered that not only did the testis eventually completely recover, but in instances where the original histology was faulty, there followed a remarkable improvement in the histological pattern. This study had been conducted on a group of inmates in an institution for the mentally deficient, and it had not been expedient to have the semen of the patients examined. The deductions were made on the histological appearances from testis biopsies taken before and at different intervals after testosterone administration.

The significance of this work was noted and among the first to apply this knowledge to the problem of infertility was Heckel.^{2,4} He reported in 1951⁵ on a small group of 5 men. Each of these patients was androgenically and anatomically normal, but all showed gross deficiency of the seminal fluid. All had spermatozoal counts below the accepted standards of fertility, and in all 5 cases biopsy showed deranged spermatogenesis. This group was given testosterone until they became azoospermic or nearly so. The testosterone was then withdrawn and examination of the seminal fluid was repeated at 4- to 6-weekly intervals.

The result of this investigation was eminently satisfactory. In 3 of the cases subsequent biopsy of the testis showed definite histological improvement in spermatogenesis, and in all the cases there occurred a remarkable rebound phenomenon. In periods varying from 4 to 7 months all the cases showed a considerable increase in the numbers of spermatozoa in the ejaculate above the pre-treatment level.

The same author⁴ then extended the study to 64 males with oligozoospermia. In 35 of these he was able to collect full data which included semen analysis and testis biopsies before and after testosterone administration. The men were physically normal except for deficient seminal fluid. They were given 50 mg. of testosterone 3 times a

week until the semen was clear of sperm or nearly so. This generally took 1.5-2 gm. of testosterone over a period of 2-3 months. The ensuing rebound phenomenon occurred with great regularity and the height of the reactivity occurred on an average between 6 and 9 months after withdrawal of testosterone. No unpleasant or undesirable general side-effects occurred during testosterone therapy or afterwards.

The actual results found in this group of 35 men bear closer analysis. In 63% of this group the spermatozoal count reached levels many times above that of the pre-treatment level. Five men in this successful group of 22 reported that their wives had fallen pregnant. In 37% the spermatozoal count was either not materially improved or was worse than before. In other words, the rebound phenomenon did not occur in 13 of 35 men. Of the 13, 8 men were much the same as before, 4 had lower counts than before, one patient who had a few sperms before treatment had none after—for as long as it has been possible to follow him. The risk of being worse off for treatment was 14%.

In interpreting these results one must bear in mind certain facts. All these men had severe oligozoospermia, with counts below 20,000,000 spermatozoa per c.c. Such cases are virtually sterile by all accepted standards. These men had been married for many years with no pregnancy resulting, and in many cases had received the usual forms of treatment. Before the discovery of this rebound phenomenon, this type of infertility was rarely amenable to any known treatment. The risk of greater infertility resulting is negligible when infertility is already almost 100%, and one should look rather with gratification at the 60% improvement and with extreme gratification at 14% complete success with pregnancy as a result.

One of many questions comes to mind: Will the improvement be permanent? The investigation is, of course, only in its infancy and this question cannot be answered in full. Heckel⁴ has, however, shown in his series that the rebound phenomenon has been maintained in almost 60% of the cases for periods from 2 to 10 months. It is futile to speculate on the probabilities until the passage of time gives us the full answer, but even if this therapy produced fertility in a reasonable number of oligozoospermic men lasting a period of many months, it would represent something very worth while.

It seems important that certain principles of treatment with testosterone should be adhered to, lest the indiscriminate use of what promises to be a valuable therapeutic aid should lead the method into disrepute.

1. The diagnosis of oligozoospermia must be established clearly by a period of observation and repeated semen analysis. Normal as well as oligozoospermic men show a considerable and 'normal' variation in the spermatozoal count.

2. The total dosage of testosterone must be guided by repeated analysis of the semen, in order to establish when to cease treatment. Testosterone is withdrawn when all or nearly all spermatozoa have disappeared from the semen.

3. A biopsy of the testis should be made before treatment is commenced. It has already been shown that only certain types of spermatogenic derangement will respond.⁴ The histological derangement must be of a reversible nature.

*Oligozoospermia denotes a diminished number of sperm in the ejaculate.

4. A man should not be subjected to testosterone therapy without due consideration of the several known causes of infertility. There is the occasional case of oligozoospermia where the cause is found and appropriate treatment can be given.

5. It is reasonable to suggest that conception by natural means should be given a fair trial before testosterone therapy is tried. Arbitrarily, one would like to suggest a period of 2 years at least.

The reason for adhering to the suggested principles is that the therapy does carry certain hazards, some of which are known, and others will undoubtedly become known in due course. For this reason, and until our knowledge of the rebound phenomenon increases, it is probably prudent to employ the method only in cases of severe oligozoospermia.

From McLeod's⁷ brilliant study of 1,000 fertile men we know that real infertility begins when the spermatozoal count drops below 20 million per c.c. The previously accepted standard of infertility at 60 million per c.c. is no longer tenable, because 25% of fathers have counts between 60 and 20 million per c.c., whereas only 5% of fathers have counts below 20 million per c.c. Thus when there exists the probable risk of 14% being worse off than before, are we justified in using the method in a group of men contributing 25% of known fathers?

The answer may lie in extended knowledge of deranged testicular histology, and it is for this reason that the suggestion is made for routine biopsy before treatment is

instituted. From the few cases which have been studied, Heller^{1,4} has provisionally suggested certain histological patterns which respond and others which apparently do not. When we are able to predict with reasonable assurance what testicular changes are reversible, then we can with greater justification employ testosterone in cases with lesser degrees of oligozoospermia and even in selected cases of azoospermia.

The haphazard use of testosterone for all males who are not able successfully to impregnate their apparently normal mates, is unscientific, will lead to confusion and disappointment, and will benefit chiefly the firms selling male hormone preparations. It should be borne in mind that the occasional case responds adversely. Instead of oligozoospermia the subject may be left with complete azoospermia.

Only critical examination and the passage of time will prove the true worth of this new treatment.

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CONGRESS 1952

COLLEGE DINNERS

The following College dinners have been arranged for Congress week:

1. *Cape Town University Graduates*. Organizer: Dr. J. R. Frylinck, Department of Surgery, Medical School, Hospital Street, Johannesburg.

2. *Guy's Hospital Dinner*. Organizer: Dr. C. Arkles, 113 Manners Mansions, Jeppe Street, Johannesburg.

Those wishing to attend must please inform the organizers concerned without delay.

VISIT TO GOLD MINES

Arrangements have been made with the Transvaal Chambers of Mines for delegates of the South African Medical Congress

and their wives to visit gold mines on Tuesday, 23 September and Thursday, 25 September 1952. As senior officials of the mines to be visited are deputed to conduct these tours, it is essential that mine managements be advised well in advance of the numbers who intend participating in these visits.

The excursions will start at 7.30 a.m. and end at 3.30 p.m. and, as the organization involved is very considerable and affects no fewer than 8 mines, the Chamber of Mines must know about a month ahead how many visitors they must expect.

Delegates who wish to avail themselves of the facilities offered by the Chamber of Mines are asked, therefore, to advise the Organizing Secretary, S.A. Medical Congress 1952, Medical House, 5 Esselen Street, Hospital Hill, Johannesburg, as soon as possible.

PASSING EVENTS

Dr. J. du Pre le Roux, Secretary for Health, has left Pretoria on an official visit to Liberia.

Congratulations to Dr. and Mrs. A. Myburgh, of Pretoria, on the birth of a daughter.

Dr. Louis F. Freed, of Johannesburg, has been elected to the Executive Committee of the newly formed Johannesburg Council for Combating Alcoholism.

SOCIÉTÉ INTERNATIONALE DE CHIRURGIE

The date of this Congress (to be held in Lisbon next year) has been altered from 6 April 1953 to 14 September 1953.

THE JOURNAL OF CLINICAL NUTRITION

The following is a list of articles scheduled to appear in early issues of the *Journal of Clinical Nutrition*:

Hypovitaminemia A by John Esben Kirk and M. Chieffi.
Psychosomatic Aspects of Dieting by Edward Weiss.
Alcoholism as a Nutritional Problem by R. J. Williams.
The Dietary Treatment of Hypertension by Irvine H. Page and A. C. Corcoran.

The Effects of Amino Acid Deficiencies in Man by A. A. Albanese.

Growth Failure in School Children: Further Studies of Vitamin B₁₂ Dietary Supplements by Norman C. Wetzel et al.

Overnutrition and Obesity by H. H. Mitchell.

Basic Research and its Application to the Field of Clinical Nutrition by Charles Glen King.

Semistarvation and Nutritional Rehabilitation, with Emphasis on Behaviour by J. Brožek.

The Therapeutic Uses of Low Fat, Low Cholesterol Diets by Frederick Urbach et al.

The Use of Formula Diets for Constant Intake (Balance) Studies by W. Kinsell et al.

REVIEWS OF BOOKS

MANAGEMENT OF THE NEWBORN

Management of the Newborn. By Arthur Hawley Parmelee, M.D. (Pp. 358. \$7.00.) Chicago: The Year Book Publishers, Inc. 1952.

Contents: 1. Introduction. 2. The Fetus. 3. Birth and Neonatal Adjustments. 4. Characteristics of the Newborn. 5. The Premature Infant. 6. Care and Management of the Newborn. 7. Disturbances Directly Due to Birth Processes. 8. Disturbances Due to Abnormal Variations of Physiologic Peculiarities. 9. Disturbances Due to Prenatal Factors. 10. Disturbances Due to Acquired Infections and Other Postnatal Hazards. Index.

The neonatal period has within recent years become the subject of increasing study and research. The persistence of a high neonatal death rate despite a constantly falling general infant mortality, has forcibly brought to notice how vital are the adjustments in this all-important epoch of life.

A clearer understanding of the complex physiological and anatomical peculiarities of the newborn is not only essential to combating the medical hazards of this period, but provides in itself a study of fascinating interest.

Within the compass of one small volume, this book covers the subject most admirably and should be of great help to all those who are entrusted with the care of the newborn. The author has based his work on long experience and close observation.

The chapter on the characteristics of the normal neonate, covering some 80 pages, is particularly outstanding.

This book is undoubtedly a valuable contribution and can be strongly recommended.

PSYCHOTHERAPY OF PSYCHOSIS

Psychotherapy of Psychosis. By Gustav Bychowski, M.D. (Pp. 336 + viii. \$5.75.) New York: Grune & Stratton.

Contents: 1. The Personality of the Psychiatrist. 2. Bleuler and His School—Their Role in Dynamic Psychiatry. 3. Special Practical Problems Presented by the Psychotic. 4. Theories of Schizophrenia. 5. Libidinal Regression, Body Ego Changes and Hypercathexis of Organs. 6. Regression of the Ego: The Phylogenetic Aspect. 7. Regression of the Ego: The Ontogenetic Aspect. 8. Ego Strength and Ego Weakness. 9. The Body Ego and Its Disintegration. 10. Defense Mechanisms of the Immature Ego. 11. The Oral Ego: Introjection and Projection of Introjected Images. 12. The Origins of the Delusion of Persecution. 13. Defense Mechanisms Used in the Handling of Affects. 14. Depersonalization. 15. Splitting and Denial. 16. Development of Delusion—The Case of Geraldine. 17. Manifestations, Dynamics, and Therapeutic Handling of Hostility. 18. Problems of Transference. 19. Problems of Interpretation. 20. Dynamic Aspects of Shock Therapy: The Structure of Psychosis. 21. Depression: Symptomatology and Classification. 22. Phenomenology. 23. Loss of the Love-Object. 24. Melancholic Depression with Schizoid Features. 25. Melancholic Depression in a Personality with a Weak Ego Core. 26. Other Forms of Depression. 27. The Manic-Depressive Cycle. 28. Mania: Dynamics of the Manic-Depressive Cycle. 29. The Psychology of Elation. 30. The Therapy of Depression. 31. Latent Psychoses. 32. Pharmacotherapy. 33. Paranoia. 34. Problems and Prospectives. Index.

The author opens with commendable hesitancy about dealing with a topic still in its infancy. He derives his rationale for psychotherapy in the psychoses from his former master Bleuler's division of the symptomatology of schizophrenia into primary and secondary, the primary being organic but the secondary due to psychological elaboration and hence on the face of it susceptible of psychotherapy. Bychowski's procedure is that of a veteran psychoanalyst giving an interpretation of the psychodynamics of various psychoses in terms of his doctrine and with apposite illustrative case histories, and following this usually by a relatively sketchy treatment of the appropriate psychotherapeutic procedures themselves.

There is little new in his psycho-analytic interpretative concepts, as may be gauged by glancing through the Contents. In the manner of his school he arbitrarily juggles about with and weaves into varying patterns the well-worn terms and clichés of psycho-analysis. For those who like this sort of thing, he does it quite well. This ideological banality and tedium is relieved by the introduction of phenomenological concepts of interpretation in the sense of Jaspers, the handling of the awareness of time in depression being done fascinatingly and with imagination. The main development of Bychowski's exposition is, however, psycho-analytic and his debt to Abraham as regards general theory is apparent and repeatedly

acknowledged. In the chapter on *Problems of Interpretation* he reviews the detailed theoretical views of other psycho-analytical thinkers, more particularly in the field of schizophrenia, paying tribute to the enormous labours and inspiration of Harry Stack Sullivan, describing the factors including warmth and sympathy in the approach of John N. Rosen and Federn, indicating the emphasis on the varying roles played by the physician in therapy of Melanie Klein, and acclaiming the original and effective technique of the Swiss psychoanalyst Madame Sechehaye, known as symbolic realization. Of the psychiatric entities the most attention by far is devoted to schizophrenia, but manic depressive psychosis, paranoia, drug addiction, latent psychoses and psychiatric changes during shock therapy also receive consideration. There is nowhere an attempt at a serious statistical evaluation of results however.

Although in the reviewer's opinion this work falls short of the requirements of science (cf. Kallmann on *Psychiatric Genetics* and Hull on *Psychological Formulation*) it can be recommended as a good and fairly well-balanced review of the subject from the psycho-analytic standpoint, by one who has devoted much time and thought to and done original work and extensive previous writing in the field.

STANDARD CLINICAL NOMENCLATURE

Standard Nomenclature of Diseases and Operations. By Richard J. Plunkett, M.D., Editor and Adaline C. Hayden, R.R.L., Associate Editor. (Pp. 1034 + xvi, with 4 illustrations. 4th ed. 60s.) London: H. K. Lewis.

Contents: 1. Schema of Classification. 2. Nomenclature of Diseases. 3. Nondisruptive Terms for Hospital Records. 4. Supplementary Terms. 5. Operations. Introduction. 6. Classification of Operative Procedures. 7. Nomenclature of Operations. 8. Anaesthesia Section. 9. Disease Index. 10. Operation Index. Appendix.

The fourth edition of this encyclopaedic work has been published for the American Medical Association. It comprises a system of classifying diseases which can claim to be a logical, clinical nomenclature.

The task was originally undertaken at the invitation of the New York Academy of Medicine in 1928, when a *National Conference on Nomenclature of Disease* was formed. The new edition has been prepared with the assistance of numerous committees in the various subdivisions of medicine, and represents one of the most comprehensive classificatory systems available.

The volume should be of inestimable assistance to medical superintendents of hospitals, records clerks, medical librarians, etc. The need to adopt some systematic form in classification was stressed in an Editorial in this *Journal* last year (29 September 1951, p. 705).

PRACTICAL THERAPEUTICS

A Course in Practical Therapeutics. By Martin Emil Rehfsuss, M.D., F.A.C.P., and Alison Howe Price, A.B., M.D. Second Edition. (Pp. 938 + xvii, with 96 plates. 114s.) London: Baillière, Tindall & Cox. 1951.

Contents: Part I. General Therapeutic Principles. Part II. Symptomatic Therapy. Part III. Treatment of Specific Disorders. Part IV. Special Treatment. Index.

This massive volume measuring 11 × 9 × 2½ inches presents the subject of therapeutics in a very attractive and readable form. It is obviously a book which practising doctors will like to have available for frequent reference. The volume will occupy a high place in the list of works on clinical therapeutics. It has many novel features, but also has many surprises.

The 17 contributors have written in much detail on many diseases. There are nearly 30 pages on the details of treatment of diabetes, with specimen diets in full. There are 73 methods listed for the stopping of hicough.

Several criticisms must, however, be made. Treatment of diseases of the nervous system is not specially considered in this book, yet, for example, the treatment of epilepsy is given; but for Parkinsonism, a disease for which several drugs are



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available, Pyridoxine is the only substance mentioned. For many diseases far too many remedies are given, and much space is taken up with lavish details of foods that may or may not be eaten. It is surprising to read that combined diphtheria-tetanus-pertussis immunization is not recommended (p. 895), that granulopaenia is a minor side-reaction produced by propylthiouracil (p. 744), and that ferric ammonium citrate is used as an anthelmintic for whipworms. The doses of oestrogens are expressed in obsolete international (rat) units. The illustrated Schafer method of artificial respiration is generally regarded as much less effective than the Nielsen methods now widely accepted in the U.S.A. Criticism must be made of the ravishing full-page female figures used in the summary charts intended to give visual aid to the study of treatment. The authors state that one well-chosen illustration is worth a thousand words. In many cases the drawings do not suggest in the slightest degree the illnesses they are meant to portray, e.g. the lovely young girl illustrating acute pancreatitis, a disease which occurs in people of an average age of 50 years (p. 280).

There is no question of the great value of this book to the general practitioner. This edition should sell as rapidly as the first.

MEDICAL ENTOMOLOGY

Grundriss Der Medizinischen Entomologie. By Prof. Dr. F. Weyer and Dr. F. Zumpt. (Pp. 150 with 66 illustrations. DM 7.50.) Leipzig: J. A. Barth. 1952.

This is the third edition of a medical entomology very much used in Germany. The book has 5 chapters dealing with the general morphology of Arthropoda, vectors, parasites and diseases, and a description of medically important Arthropoda, their life history and significance, all arranged according to their systematic position. Lastly come methods of control, and how to collect and preserve the animals.

Apart from minor objections to the account of insect morphology and the rather short reference list, this appears to be a good book, which ought not to be missing from the shelf of any medical entomologist. It is clear and scholarly in the way it presents its subject, thus giving the beginner a useful introduction. All definitions are stressed with care. Most interesting reading is the chapter about the control of pests, because it gives an account of the effect of the new contact insecticides on pests as well as on man and his livestock.

In spite of the language difficulties, the book ought to find a good market in South Africa.

PATTERNS OF SEXUAL BEHAVIOUR

Patterns of Sexual Behaviour. By Clellan S. Ford, Ph.D. and Frank A. Beach, Ph.D. With an Introduction by F. A. E. Crew, M.D., D.Sc., Ph.D., F.R.S. (Pp. 807 + vii with 16 figures and tables. 22s. 6d.) London: Eyre & Spottiswoode (Publishers) Ltd. 1952.

Contents: 1. The Task and the Methods. 2. The Nature of Coitus. 3. Types of Sexual Stimulation. 4. Circumstances for Coitus. 5. Attracting a Sex Partner. 6. Sexual Partnerships. 7. Homosexual Behaviour. 8. Relations between different Species. 9. Self-Stimulation. 10. Development in the Individual. 11. Feminine Fertility Cycles. 12. Other Physiological Factors in Sex Behaviour. 13. Human Sexual Behaviour in Perspective.

This valuable and objective account of sexual behaviour has been written by an anthropologist and a psychologist on the staff of Yale University. The introduction is by Prof. F. A. E. Crew, at present Professor of Public Health and Social Medicine at Edinburgh University. Professor Crew is, of course, a biologist of international repute whose views are well known to the medical world.

It is important to appreciate that a comparative study of sexual behaviour is often the most illuminating approach to an understanding of human problems. This book is, in Professor Crew's words, 'a model of scientific writing', and its analysis of almost 200 contemporary human societies gives some insight into the careful and unemotional manner in which the authors have tackled this important task.

The volume is comparative in respect of human societies, and it also provides a foundation of knowledge about non-human societies.

The monograph undoubtedly imparts to the reader an appreciation of the need to view sexual behaviour in a broad

perspective, an attitude of mind particularly necessary in a society such as ours which is only beginning to emerge from the inhibitions and the taboos which unfortunately still surround this topic.

GYNAECOLOGY

Die Vaginalen Bauchhöhlen-Operationen. By Prof. Paul Werner and J. Sederl, Vienna. (Pp. 52 + 120 pages of illustration.) Vienna: Urban and Schwarzenberg. 1952.

Contents: 1. Introduction. 2. Instruments and preparation for operation. 3. Vaginal opening of the abdominal cavity. 4. Vaginal hysterectomy. 5. Total vaginal hysterectomy of the myomatous uterus (Morcelement). 6. Vaginal panhysterectomy. 7. Corpus resection and vaginal subtotal hysterectomy. 8. Vaginal myomectomy and removal of the ovarian cysts per vaginam. 9. Vaginal operation for abdominal pregnancy. 10. Vaginal tubal sterilization. 11. Vaginal antifermentation of the uterus by shortening and fixation of the round ligaments. 12. Vesico-vaginal interposition of the uterus. 13. Opening of abscesses through the posterior fornix.

The late Professor Wertheim's only surviving assistant, Prof. Paul Werner, assisted by his co-worker Dr. Julius Sederl, has just brought into print this excellent work. The book is written in simple language and the printers must be congratulated on the quality of the paper, the exquisite printing and the superb reproduction of the instructive illustrations.

The author, whose brilliance as an operator is well known in and outside Vienna, describes briefly and clearly every step in the operations mentioned and his illustrations, prepared from actual operations on the living, make this book an outstanding contribution to vaginal surgery.

The vaginal approach to the abdominal cavity is made easy to the inexperienced in this department of surgery and fascinating to the gynaecologist who has been in the habit of choosing the abdominal route.

Attention is drawn to the advantages of the vaginal route such as the low mortality and morbidity, the painless, easy and rapid convalescence, the absence of post-operative shock and the lower incidence of post-operative thrombosis and pulmonary embolism as compared with laparotomy.

All this becomes particularly evident when one has to deal with the enormously fat patient and the abdominal route becomes technically impossible or too dangerous.

Bowel activity remains practically undisturbed after vaginal operations. Werner's book describes vaginal technique to perfection. Not even is the care of the stumps forgotten—an important factor in avoiding complications.

DUKE-ELDER'S OPHTHALMOLOGY

Text-Book of Ophthalmology. By Sir Stewart Duke-Elder, K.C.V.O., M.A., LL.D., D.Sc. (St. And.), Ph.D. (London), M.D., F.R.C.S., Hon. D.Sc. (Northwestern), D.M. (Utrecht), F.R.C.S. (Edin.), F.A.C.S. Vol. V: The Ocular Adnexa. (Pp. 4631-5713 + xxxii, with 1181 illustrations, including 32 in colour. 90s.) London: Henry Kimpton. 1952.

Contents: Volume V: The Ocular Adnexa. Section XVII: The Ocular Adnexa. Chapter I.VI. Developmental Anomalies of the Ocular Adnexa. Chapter I.VII. Diseases of the Lids. Chapter I.VIII. Diseases of the Lacrimal Apparatus. Chapter I.IX. Diseases of the Orbit. Chapter I.X. Diseases of the Para-Orbital Regions. Index.

Surprisingly soon after Volume IV, one has the pleasure of studying another instalment of Duke-Elder's monumental work.

The first chapter, dealing with anomalies of development of lids, lacrimal apparatus and orbit, provides a variety of conditions ranging from mild abnormalities, such as blockage of the naso-lacrimal duct, interesting rarities such as Marcus Gunn's 'jaw winking', to gross defects caused by amniotic bands, and dysostoses. In addition to illustrations, numerous pedigrees are provided.

The chapter devoted to the diseases of the lids stresses the complications of pathology caused by the meeting of the skin, fibrous layer and conjunctiva. This section naturally includes much dermatology, and the importance of treating associated skin lesions is emphasized. There is much of general medical interest here, including an excellent account of motor disorders of the lid.

The lacrimal apparatus provides, once again, much of general interest. Mikulicz's syndrome, and 'mixed' tumours

are discussed fully, as well as conditions more exclusively in the province of ophthalmologists such as epiphora.

The great American neuro-surgeon, Dandy, is mentioned, in the foreword to the section on the orbit, for his transcranial orbital surgical approach. The influence of the lack of lymphatics and the limiting action of the fascial membranes on the pathology of orbital inflammation is well described. Orbital involvement in general diseases, the difference between exophthalmic goitre and exophthalmic ophthalmoplegia, and a discussion on the proximate and ultimate causes of exophthalmos, combine to make this section of great interest.

The final chapter deals with the nose, sinuses, ears and teeth. For instance, one is reminded that the first sign of many naso-pharyngeal neoplasms, diplopia, may bring the patient to the ophthalmologist.

The whole work is enhanced by the excellent illustrations, including those of many pathological sections. Full references to relevant literature follow each sub-section.

The general standard of printing and reproduction is in keeping with that which one now associates with all Kimpton publications.

NAUTICAL MEDICINE

James Lind, Founder of Nautical Medicine. By Louis H. Roddis. (Pp. 176 + xi, with 8 illustrations. 21s.) London: William Heinemann.

Contents: 1. The Early Life of Lind and the Making of a Physician in Eighteenth Century Scotland. 2. A Surgeon in the Navy of King George II. 3. Scurvy—The Sea Plague. 4. The Conquest of Scurvy. 5. Laying the Foundations of Naval Hygiene. 6. Fresh Water and Salt Water. 7. A Pioneer of Tropical Medicine. 8. The First Physician of the Royal Hospital at Haslar. 9. Death, Honors and Appraisal of Achievement.

In writing about the life and times of James Lind, Roddis (a naval surgeon) attempts to remedy a gap in medical biography. Lind's magnificent contributions to present-day naval hygiene were probably overshadowed by the work of Jenner, the Hunters and other great men of his time.

This Scottish naval surgeon of the eighteenth century is perhaps best known for his convincing research on scurvy on board the *Salisbury* in 1747. Ships could not be sailed or fought by sick and dying seamen, and it was Lind, more than any other man, who sent the British Navy into many of its decisive battles of the eighteenth and nineteenth century with all its manpower available. Scurvy, the 'Black Death of the sea', was virtually eliminated.

More convincing of his genius were some of his other medical contributions. He knew of the prevention and treatment of malaria before the part played by the mosquito was known. Ship typhus prevention and the distillation of sea water were two more less well-known contributions. The man has justly been called the 'father of naval hygiene'.

Those whose interests lie in medical history, nautical medicine or in a medical work that reads like a novel, should make a place for this book on their shelves.

NEUROLOGY AND PSYCHIATRY: 1951

The 1951 Year Book of Neurology and Psychiatry (November 1950–October 1951). Edited by Roland P. Mackay, M.D. and Nolan D. C. Lewis, M.D. (Pp. 556, with 109 illustrations. \$5.50.) Chicago: The Year Book Publishers, Inc. 1952.

Contents: Part I. Neurology. 1. Introduction. 2. Physiology. 3. Pathology. 4. Trauma. 5. Infectious Diseases. 6. Vascular Disturbances. 7. Degenerative Diseases. 8. Tumors of the Brain. 9. Tumors of the Spinal Cord. 10. Epilepsy. 11. Cranial and Spinal Nerves. 12. Diagnosis and Therapeutic Methods. Part II. Psychiatry. 1. Introduction. 2. General Topics. 3. Child Psychiatry. 4. Schizophrenia, Affective Disorders and Miscellaneous Reactions. 5. Organic Disorders and Toxic Reactions. 6. Psychoneuroses and Psychosomatic Disorders. 7. Therapy. Index.

With the continually increasing numbers of medical journals it becomes almost impossible to keep up with the literature, even in a single speciality, so that some kind of annual compendium becomes essential for both the general and the specialist physician. The *Year Book* series are certainly amongst the most attractive and complete of the various excerpts and have been re-issued in the format which was started last year.

This year's edition of the *Neurological and Psychiatric Sections* has incorporated the *Neurosurgical Section* within these two headings, and although the resignation of so distinguished an Editor as Percival Bailey must be regretted, nevertheless Dr. Mackay and Dr. Lewis are both perfectly competent to judge and comment upon surgical procedures. Indeed, the commentaries in general, brief as they are, make a useful and balanced contribution to the *Year Book's* abstracts and prevent claims from appearing too extravagant without altering the conclusions of the original articles.

Amongst the most important advances reviewed are those of angiography, psycho-surgery and work on psychomotor epilepsy and on the virus infections of the nervous system. It is a pity that more space has not been found for neuro-physiological advances, especially the electro-physiological experiments, but in general it must be admitted that the most important articles in most fields of neurology and psychiatry have been covered. The width of the ground reviewed may be judged from the fact that the *Neurological Section* contains 160 abstracts from American sources, 50 from Great Britain, 5 from the British Empire, 40 from various continental countries and 3 from South America.

Once again the *Year Book* appears in an attractive binding, well printed and with excellent illustrations. The absence of advertising matter is to be applauded, while the *Year Book* itself is undoubtedly a virtual essential for anyone interested in current events in neurology or psychiatry.

WILLIAM SMELLIE

William Smellie: The Master of British Midwifery. By R. W. Johnstone. C.B.E., M.A., M.D., Hon. LL.D. (Pp. 139 + viii, with 30 illustrations. 20s.) Edinburgh and London: E. & S. Livingstone Limited. 1952.

Contents: 1. The Setting of Smellie's Life. 2. The Early Years. 3. The Country Practitioner. 4. From Lanark to London. 5. Man-Midwife and Teacher. 6. Smellie's 'Machines' and Antenatal Teaching. 7. The Crusader and his Antagonists. 8. The Treatise. 9. The Treatise (continued). 10. The Treatise—Volumes II and III—General Features. 11. The Treatise—Volumes II and III. 12. The Anatomical Tables. 13. Burton Versus Smellie. 14. Smellie's Obstetrical Instruments. 15. The Last Phase and After. 16. Autobiographical Fragments. 17. Smellie's Greatness and Posthumous Fame. Index.

This interesting biography of a Scots country practitioner who became the most distinguished obstetrician of his day, and who has been named as the 'Master of British Midwifery', has been well told by Professor Johnstone.

Smellie, a native of the town of Lanark with 2,000 inhabitants, was born in 1697 and educated at the local Grammar School. To members of the Medical Council and others, it will come as a surprise that he commenced practice in his native town only after serving an apprenticeship to a Glasgow doctor and without any 'letters after his name'. Not till 12 years after he commenced practice was he admitted as a freeman of the Faculty of Physicians and Surgeons of Glasgow; and later he was granted, without examination, the M.D. of Glasgow University.

It is a remarkable fact that within an area of a few miles, and within a few years, Smellie, Cullen John and William Hunter were born.

During his long horse-back journeys he pondered over his obstetrical difficulties, and later wrote valuable notes on his cases. Some of these are recorded in his *Treatise on the Theory and Practice of Midwifery*, a copy of which is in the Historical Section of the Medical Library of the University of Cape Town.

He tried forceps and fillets and noose and other contrivances, but felt dissatisfied and decided on the equivalent of a post-graduate course in London and Paris. He set out on his 13-day horse-back journey to London 'to learn more'. Eventually he took the bold step of setting up in Soho with the object of practising and teaching midwifery. Everyone knows the Smellie-Veit technique for delivery of delayed breech presentations, but his ante-natal teaching, ingenious 'machines' and other devices for teaching doctors and midwives the mechanisms, are not so well known. His forceps, his cochet, his perforator were all in advance of those in use in his day.

He had a hard fight to establish himself as a 'man midwife' and came in for criticism from his professional colleagues, but

he triumphed in the end. He was not a man who in any way realized his own greatness.

Professor Johnstone records some of the remarkable tributes given to Smellie. von Siebold wrote: 'Smellie was the first man to appreciate properly the wonderful way in which nature manages the business of birth.' Fasbender calls him 'one of the most important obstetricians of all ages and all countries'. Professor Miles Phillips writes: 'No man ever advanced in his own lifetime, knowledge of the theory and practice of midwifery to an extent comparable in any way with that achieved by Smellie'.

This is a book to read and treasure.

PAEDIATRIC ADVANCES

Advances in Pediatrics, Volume 5. Edited by S. Z. Levine. (Pp. 273. \$7.00.) Chicago: The Year Book Publishers, Inc.

Contents: 1. Advances in the Treatment of Bacterial Meningitis. 2. The Nephrotic Syndrome in Children. 3. The Relation of Vitamin K Deficiency to Hemorrhagic Disease of the Newborn. 4. Angiocardiographic Studies in Children. 5. Iron Metabolism in Infants and Children: Serum Iron and Iron-Binding Protein—Diagnostic and Therapeutic Implications. 6. BCG Vaccination.

This valuable series of annual reviews has seen a change of publisher and now comes out under the distinguished imprint of the Year Book Publishers, Inc.

The limitation of the survey to half-a-dozen important topics is a wise policy, particularly as the subjects are covered by writers of international repute and experience.

It is clear from the Table of Contents that all the themes in the present volume are of the greatest interest and importance to the paediatrician as well as the general practitioner.

Wallgren's account of BCG vaccination, however, covers a contentious and controversial field with certain interesting and important omissions. Serious objections which have been raised by American writers such as Myers are not mentioned by Wallgren nor is weight given to the discouraging experiences of veterinarians who have failed to find in BCG vaccination the protection they expected. The statement at the present time that a vaccine prepared from vole tubercle bacilli should be as suitable as BCG for prophylactic purposes has a certain obsolete ring to it in 1952.

This is, nevertheless, a most attractive contribution to medical literature, well worthy of serious study.

THE TUBERCLE BACILLUS AND THE LABORATORY

Tubercle Bacillus and Laboratory Methods in Tuberculosis. By M. A. Soltys, Ph.D., D.M.Vet., in collaboration with C. A. St. Hill, M.B., Ch.B. and I. Ansell, M.D., M.R.C.P. (Pp. 212 + vii, with illustrations. 20s.) Edinburgh and London: E. & S. Livingstone Limited, 1952.

Contents: Part I. Tubercle Bacillus. 1. History of the Tubercle Bacillus. 2. The Morphological Characteristics of *Mycobacterium Tuberculosis*. 3. The Chemical and Antigenic Structure of *Mycobacterium Tuberculosis* and its Biological Properties. 4. Growth and Metabolism of Tubercle Bacilli. 5. Cultural Characteristics of Tubercle Bacilli. 6. Virulence. 7. Pathogenicity of Tubercle Bacilli in Experimental Animals. 8. The Resistance, Viability, and Stability of *Mycobacterium Tuberculosis*.

Part II. Laboratory Methods of Tuberculosis. 9. Collection and Preparation of Specimens for the Demonstration of the Tubercle Bacillus. 10. Methods of Homogenisation and Concentration. 11. Methods of Staining. 12. Cultural Methods. 13. Inoculation of Experimental Animals and Post-mortem Examination. 14. Serological and Other Laboratory Tests in Tuberculosis. 15. Chemotherapy in Tuberculosis. 16. Tuberculin and its Application. Index of Authors. Subject Index.

This volume of 212 pages is divided into 2 main parts. The first, detailed above, deals in general with the bacteriology of the tubercle bacillus and consists of 8 chapters, each of which comprises a review of the literature under the respective subject headings. The information is provided in concise form but is extensive, and a full bibliography is given at the end of each chapter.

The second part, devoted to the laboratory methods of tuberculosis, comprises the larger portion of the book and here the subject matter is dealt with in more detail. All of the older and most of the more recent methods are described. The Middlebrook and Dubos tuberculin haemagglutination test is given fully, but the haemolytic modification has been omitted. This, however, is probably an unjust criticism, as the bibliography is so extensive that the reader can obtain all accessory information from the references.

Very few words are wasted in the whole volume with the exception of a paragraph or two in the section under post-mortem examination of experimental animals, where the necessity for cleansing and sterilizing of infected post-mortem instruments is unnecessarily stressed as the book is obviously intended for bacteriologists. This is the only (and quite negligible) criticism the reviewer can offer.

The monograph is essential for all bacteriologists and is a mine of information on all aspects of laboratory methods in tuberculosis.

CORRESPONDENCE

SELF-PALPATION AND BREAST CANCER

To the Editor: Professor Saint is the senior Professor of Surgery in South Africa, and as such, should command considerable respect for his views. I was therefore amazed that he should express opinions which are irrelevant, inaccurate and hopelessly out of date even on the clinical aspect of cancer of the breast.

His views on the role of the radiologist in carcinoma of the breast are completely out of date and not in keeping with the enlightened attitude in such centres as Edinburgh, Stockholm and London. At Edinburgh, Professor McWhirter sees every breast before operation. Similarly in Stockholm at the Radiumhemmet (Berven, 1939) 2 radiotherapists see every breast cancer with a surgeon before operation and at the Royal Cancer Hospital (London), Ledlie (1948) states that since 1937 the breast cases have been seen in consultation before operation with the radiologist. Professor Saint is therefore only 15 years out of date on this aspect.

The majority of breast cancers are seen beyond stage 1. It follows therefore that even in those cases where the radiologist is not called into consultation before operation, he nevertheless sees the majority of breast cancer patients at some stage or other for therapy. In any case, most careful surgeons (realizing the difficulty of being certain that a case is really stage 1) send even the clinical stage 1 cases for radiotherapy.

It must also be obvious that the radiologist's association with the breast cancer patient is on a far different level from that of the surgeon who only sees the patient at a consultation before the operation, then at the operation when the patient is under an anaesthetic and possibly several times in the succeeding fortnight.

The radiologist, on the other hand, is in contact with the breast cancer patient during the post-operative radiotherapy period—which may last from 3–6 weeks—during the subsequent follow-up sessions and ultimately during the heart-breaking period when he may have to chase secondary deposits in skin, bone or elsewhere for the remainder of the patient's life, which may be a number of years.

During this period the radiologist gets to know the psychology of the patient far better than does the surgeon. Yet Professor Saint questions the right of the radiologist to give an opinion on the subject!

Professor Saint regards the figures I quoted as irrelevant, but the incidence of cancer of the breast and the relative numbers in stage 1 and subsequent stages are the essence of the problem. Statistics of lunacy in the U.S.A. taken from 'lay' reports he apparently regards as more relevant to the cancer problem.

He states he has seen a case of haematoma of the breast which he regarded as due to palpation. He does not state that he has seen more than one such case. 'Women's breasts

are very frequently bumped and bruised' (Ewing, page 594). It is quite possible for a woman to attribute a bruise to her own palpation when it may have been due to some accidental trauma. I would suggest that any woman who causes a haematoma by self-palpation is in need of a psychological examination or a blood count.

One is not a little amazed that, on the clinical aspects of breast cancer, Professor Saint should be as out of date as in his attitude towards the radiologist. He states he would 'remind' me that the tendency is for the most malignant cases to be in those under 40 years of age. Analyses during the last 10 years of large series of cases indicate that this view is incorrect, if one excludes carcinoma of the breast in the pregnant or in the lactating woman. Nohrman (1949) in a study of 1,042 cases; Smithers (1952) in a study of 1,777 cases; Truscott (1947); Scarff and Handley (1939); Bloom (1950); Ackerman and Regato (1947), and many others show that the prognosis is not worse under 40 than over 40 years of age. Smithers (1952) who makes an exhaustive study of cancer of the breast, summarizes (on page 44) as follows: 'There is some evidence of prognosis varying with age, being comparatively good in younger women, poor in women in their fifties, improving again in the sixties and seventies, being bad in the eighties.'

Professor Saint's reminder to me would therefore appear to be out of place. It was only intended to show the ignorance of myself—a radiologist. What he has shown instead is that his lecture notes are at least 13 years out of date. In any case, even if he were correct, it would be an argument in favour of self-palpation below the age of 40, as Haagensen (1952) advises and it is not an argument against self-palpation of the breast.

In your Editorial on 26 March you credit Professor Saint with the view that trauma associated with excessive palpation may precipitate the development of malignancy. There is not the slightest evidence that trauma of this type could give rise to carcinoma of the breast.

The noted statistician, Dr. Johannes Clemmesen (1948). Saner (1946), Willis (1948) and many others, all indicate that although injury is often blamed as the cause of primary tumours in the breast, in most cases it is purely coincidental.

Professor Saint's attempt to establish a relationship between the increase of 20% in mental disease in the United States and such programmes as regular self-palpation of the breast for cancer, was probably not intended to be taken seriously and does little justice to the American Cancer Association which has built up an enormous organization and which has probably done more, and is doing more, than the whole of the rest of the world put together, towards combating cancer. The problem is whether it would be wise to get earlier diagnosis of cancer of the breast by self-palpation, at the risk of causing an indefinite number of women unnecessary anxiety.

Gibes at radiologists, and an attitude towards them given up by enlightened surgeons 30 years ago, out-of-date views on the etiology and virulence of cancer of the breast, are quite irrelevant and do not in any way help to solve the problem.

Since this correspondence started in the *Journal*, an article on *Self-Examination of the Breasts* by C. V. Haagensen has appeared in the *Journal of the American Medical Association*, 24 May 1952, page 356. Haagensen is a distinguished surgeon of Columbia University. He has published with Dr. Stout, the pathologist, a number of articles on cancer of the breast during the last 20 years. He is not a mere radiologist! He deals adequately with all the controversial points and is a strong advocate of self-examination of the breast. I would suggest that Professor Saint should read this article by his surgical colleague, and then let us have his views.

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Maurice Weinbren.

X-ray Department,
 Chamber of Mines Hospital,
 P.O. Box 774,
 Johannesburg.
 10 July 1952.

REGISTER OF CANCER RESEARCH WORKERS

To the Editor: The International Cancer Research Commission of the Union Internationale Contre le Cancer has decided to establish and maintain a register of organizations and doctors working on cancer throughout the world, as well as the projects on which they are engaged.

My Association has been asked to furnish information in respect of South Africa, and I shall be glad, therefore, if hospitals and laboratories undertaking cancer work would send details about the following:—

1. The name of the hospital or organization.
2. How it is maintained—whether by private means or Government allowances.
3. A list of the research workers and their category. Please also state who provides their remuneration.
4. The material used and the type of research undertaken.
5. The problems which are being dealt with at present and the future programme.

It would be appreciated if all concerned would furnish this information to P.O. Box 2000, Johannesburg, as soon as possible.

M. Collis,
 Secretary.

The National Cancer Association of South Africa,
 Medical House,
 5 Esselen Street,
 Johannesburg.
 10 July 1952.

PUBLIC HEALTH AND INDUSTRIAL HEALTH: POST-GRADUATE INSTRUCTION

To the Editor: The Royal Institute of Public Health and Hygiene conducts recognized Courses of Instruction (starting annually in March and October), for the examinations of the Conjoint Board of the Royal College of Physicians of London and the Royal College of Surgeons of England, for the Certificate in Public Health.

These lead to Courses (commencing in January and August) for the Diploma in Public Health and, similarly (in February and July) for the Diploma in Industrial Health.

Students are also prepared for the Diploma in Industrial Health examinations of the Society of Apothecaries of London. Any of the Courses may be taken whole-time or part-time. They consist of both lectures and visits.

Candidates desiring a Course for either the Diploma in Public Health, or the Diploma in Industrial Health of the Conjoint Board, are required by them to produce evidence of being in possession of a recognized Certificate in Public Health.

For the Certificate in Public Health, lectures are given by specialists on the various sociological aspects, and in the Diploma in Public Health, the practical work is carried out at a County Borough.

The Diploma in Industrial Health Course entails visits to all types of factories and to coal mines, etc.

Further information, entry forms and prospectuses may be obtained from the Secretary of the Institute, 28 Portland Place, London, W.1, or from the Dean at 23 Queen Square, London, W.C.1.

H. H. Gerrans,
 Secretary.

The Royal Institute of Public Health and Hygiene,
 28 Portland Place,
 London, W.1.
 24 July 1952.

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P. 16

City of Bloemfontein

VACANCY: HOUSE SURGEON

Applications are invited for appointment as house surgeon at the Isolation Hospital, Tempe, at a salary of £20 per month plus free board and lodging, plus temporary cost-of-living allowance.

The appointment will be for the period September to November 1952, and the successful applicant will be required to assume duty on 1 September 1952.

The Isolation Hospital is recognized by the South African Medical Council as an institution for compulsory internship.

Applications stating age, sex, race, marital state and qualifications must reach the undersigned not later than 12 noon on Thursday, 28 August 1952.

Canvassing for appointment will be a disqualification.

P. R. Joubert
Town Clerk
8643

(Notice No. 104-6/8/1952)

University of Cape Town

POST-GRADUATE MEDICAL SCHOLARSHIP

Applications are invited for the Baron Hartley Scholarship of approximately £300 per annum for the study of medicine or surgery at any hospital or university in the British Empire. The scholarship is available from 1953 and may be held for a period of three years. Candidates must be graduates in medicine of the University of Cape Town of not less than two years' standing.

Forms of application and conditions of award may be obtained from the Registrar, University of Cape Town, Private Bag, Rondebosch. Applications close on 31 October 1952.

A. V. H. Carter
Registrar

7 August 1952

Public Service Commission

VACANCIES IN THE PUBLIC SERVICE

1. The attention of Medical Practitioners, registered with the South African Medical and Dental Council, is drawn to an advertisement appearing in the *Government and Provincial Gazettes* of this week, inviting applications for the under-mentioned posts:—

Post	Department	Salary Scale
Medical Officer (Leprosy Research)	Health (Pretoria)	£1,200 × 50—1,350
District Surgeon, Grade II	Health (Nylstroom)	£1,000 × 50—1,200
Medical Officer	Health (Mental Hospital Service)	£900 × 50—1,150
Medical Officer	Health (Durban)	£900 × 50—1,150
District Surgeon, Grade III	Health (East London and Nylstroom)	£900 × 50—1,150
Medical Officer	Labour (Cape Town)	£900 × 50—1,050

2. In addition to salary a cost-of-living allowance at the rate of £320 per annum (married) and £100 per annum (single) is payable at present.

3. It is emphasized that full and detailed particulars of qualifications and previous experience must be furnished but original certificates and testimonials should not be submitted. Application forms (Z.83 and P.S.C. 8 (a)) are obtainable from the Secretary, Public Service Commission, Pretoria, to whom filled-in forms must be addressed.

4. The closing date for the receipt of applications is 6 September, 1952.

36582

The Medical Association of South Africa Die Mediese Vereniging van Suid-Afrika

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PRAKTYKE TE KOOP : PRACTICES FOR SALE

(1003) Transkei. Well-established dispensing practice. Total cash receipts 1951, £3,311. D.S. and M.O.H. appointments. Large well-built house for sale at £3,300. Premium required, £1,500.

(1010) Cape Town. Nucleus of practice with excellent scope for expansion. Average annual receipts £1,100. Premium required, £850, which includes drugs, few instruments, half-share furniture. Consulting rooms shared with specialist.

(1016) Eastern Province. Unopposed solus practice. Average annual receipts, £2,471. Premium for goodwill, £1,000. Drugs, furniture and instruments offered at £190. Terms available. Attractive modern home to rent at £8 10s. p.m. Rental roomy surgery, £3 p.m.

(1048) In Eastern Cape industrial and seaport town, expanding practice—cash receipts 1951-52, over £5,000. Long introduction offered. Owner specializing. House with attached consulting room available to purchase or to rent. Terms can be arranged.

(992) South-Eastern Cape hospital town. Premium required £1,500, which includes drugs, furniture and instruments worth approximately £1,350. Flat plus surgery to let at £6 p.m. Gross average annual cash takings, £2,500. Easy terms. Owner wishes to specialize.

(1101) Coastal city. Better-class general practice. Gross annual receipts £2,200. Premium required £1,750. Terms possible. Practice is expanding.

(1099) Well-established unopposed East Griqualand practice. Three good appointments. House to let at nominal rental. Gross cash takings for year ending December 1951 were £3,668. Premium required, £2,150. Terms available. Excellent opportunity for English-speaking doctor.

(Pr/553) Noord-Kaapland. Uitstekende praktyk vir geneesheer wat snwyker doen. Inkomste £6,000 per jaar. Premie verlang £3,500. Volle besonderhede op aanvraag.

ASSISTENTE/PLAASVERVANGERS VERLANG ASSISTANTS/LOCUMS REQUIRED

(1067) Small Transkeian village. Assistantship with definite view to partnership. Single man would be preferred. Initial salary offered £60 p.m. all found.

(1083) Transkei. As soon as possible for 1 month with the possibility of permanent assistantship. Good salary offered for experienced locum.

(1105) Western Province hospital town. Bilingual assistant who will be interested in the welfare of working-class patients.

(1106) South-Western District. Bilingual locum/assistant with a view to partnership, required as soon as possible.

JOHANNESBURG

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Mediese Huis, Esselenstraat 5. Telefoon 44-9134-5, 44-0817

PRAKTYKE TE KOOP : PRACTICES FOR SALE

(Pr/S34) Progressive Transvaal town dispensing practice. Average gross income £3,500 p.a. Excellent surgical facilities. Owner going overseas.

(Pr/S39) Pretoria practice. Gross annual income, £3,200 to £3,500. Premium required £1,750. No house for sale. Full details on application.

(Pr/S46) O.F.S. dispensing practice. R.M.O. and M.O.H. appointments. Average monthly takings £260. House to let at £10 p.m. Premium required £1,000, which includes instruments, drugs and furniture. Cash is preferred, but terms could be discussed.

(Pr/S47) Johannesburg. old-established practice. Premium required £2,000. Surgery furniture and X-ray £650. Terms will be considered. Please apply for full details.

(Pr/S51) Transvaal hospital town dispensing practice. Gross income over £6,000 per annum. It is essential that this practice be worked by two men, one to be a surgeon. Premium required £3,500, and terms could be arranged. Practice can only be sold if house and surgery are bought for cash. Details on application.

(Pr/S48) Northern Rhodesia. Unopposed solus dispensing practice. Annual gross takings £5,000 (cash £3,500 and accounts £1,500). No bad debts, very little night work. Premium required £1,600. Drugs and furniture on valuation. Surgery buildings for sale or for hire. Will suit doctor who is not interested in city life.

(Pr/S52) Progressive Transvaal hospital town. Practice with excellent scope for expansion. Premium required £600 and terms could be arranged. Premium includes drugs, furniture and instruments valued at £160.

(P/O12) Partnership share in good-class Johannesburg practice. Average annual income £4,000, of which 75% cash and balance on terms.

DURBAN

112 Medical Centre, Field Street. Telephone 24049

PRACTICES FOR SALE : PRAKTYKE TE KOOP

(PD10) General practice, Natal inland city. European and non-European patients. Scope for midwifery and surgery. Premium required £1,250, cash preferred, but terms will be considered. For immediate sale.

(PD13) Natal Lower South Coast practice, near Pondoland border, suitable for retired doctor. Area developing and large Police holiday camp in vicinity. Excellent climate and very good fishing. Premium required £400, includes good stock of drugs and dressings, instruments and dispensary furniture. House for sale £1,800, including stand of one-third morgen. Bond available. For immediate sale. Owner having taken a full-time appointment.

LOCUM REQUIRED

From 27 August to 21 September. Natal village, 25 miles from Stanger. £2 2s. per day, all found, plus £5 car allowance. Woman doctor preferred, but must possess own car. District Surgeoncy and Native practice. No surgery or midwifery, and no night work.

Natal Midlands village. Month of November. £2 12s. 6d. per day, free board and lodging. Petrol and oil supplied. Single man preferred, but not essential. Mixed country general practice. No midwifery or major surgery. Hardly any night work. Dispensing of stock mixtures only. Native interpreter employed.

Wanted

Assistant in partnership practice in Vereeniging. Must supply own car. £2 10s. per day, plus £20 per month car and petrol allowance.

Write to 'A. M. U.', P.O. Box 643, Cape Town.

Post Wanted

Distinguished lady with experience seeks post as doctor's receptionist in Johannesburg. Good references. Write to 'A. M. V.', P.O. Box 643, Cape Town.

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